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THE SURGICAL CORRECTION OF CONSTRICTIVE PERICARDITIS

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THE operation for chronic constrictive pericarditis, whose ill effects stem from the concomitant compression of the heart and its large vessels either by contracting scar or by the pressure of fluid confined within a rigid-walled envelope, has yielded varying results, some disappointing and some spectacularly brilliant. Twenty-two deaths on the operating table in 265 reported cases (Table I) provide abundant proof of the hazardous nature of the operation and 48 early postoperative deaths further testify to the extreme gravity of the disease. All the more gratifying, therefore, are the 118 cases reported as restored to normal health, and the 44 cases reported as improved.

The following important factors contributed to the success of the operation: its application in young individuals in whom other organs were normal and in whom liberation of the compressed heart was the only correction necessary; the availability of intratracheal anesthesia, and such adjuncts in after-care as oxygen, transfusions, and antibiotics; an adequate exposure of the heart which permitted ready access to critical areas for the removal of the offending scar; and the courage and technical skill of the operating surgeon which enabled him to pursue the operation until adequate decompression of all critical areas had been achieved.

Factors contributing to poor results were such considerations as the etiology of the primary pericarditis, whether tuberculous or pyogenic in origin, the former being strikingly dangerous in the advanced chronic stage; the selection for operation of exceedingly ill patients whose only hope lay in liberating the hampered heart but who died on the operating table or within a few hours after operation; technical difficulties leading to lacerations in the thin walled auricle or in the myocardium of the right ventricle with fatal hemorrhage; inability to remove the scar because of penetration of cardiac musculature by calcium deposits; inadequate removal of scar necessitating secondary operations; failure to remove the scar over critical areas such as the inferior and superior vena cava; technical difficulties imposed by the type of operative exposure of the heart; and lastly the postponement of a correct diagnosis until changes had occurred in the cardiac musculature so that liberation of the compressed heart resulted in overdilatation of attenuated and atrophied myocardium and in circulatory failure.

Considerable difference of opinion has been expressed by various writers as to what really are critical areas: Schmieden (30, 31), whose excellent articles stimulated internists to diagnose and surgeons to operate upon this heretofore rarely recognized entity, states:

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TABLE I

Author	Etiology			Mortality			Results		
	No. of cases	T.B.C.	Non TBC	At operation	Postoperative	Late	Not improved	Improved	Cured
Heuer and Stewart survey of literature to 1939 (19)	143			19	28	13		25	50
Blalock and Burwell 1941 (6)	20	14	6		4 1	3			7 5
Harrington 1944	24	5	19	1	2 3			2 7	1 8
Heuer and Stewart (18)	7* 11			0	0	3**	3**	3* 4	4* 4
Beck	46			1	8	4		2	31
Sellors	5	3	2		1			1	1 2
Harrison and White	12* 16	3 2	9 14	1* 1	2* 1	3* 2		1* 3	5* 9
Total	265			22	48	25		44	118

*Cases included in the survey of Heuer and Stewart (19)
**The same patients

"The operative technique is based upon the following fundamental principles: (1) liberation of the left ventricle first, in order that it can receive and immediately deliver to the systemic circulation the increased output of the right ventricle following its subsequent decortication and thus avoid the right-sided venous congestion that would otherwise occur; (2) freeing of the right ventricle, which then usually dilates more efficaciously and beats stronger. . . . Owing to the thin wall of the auricles, these should not be freed. . . . In order to avoid the development of deficiency of the auriculoventricular valves, thus leading to the immediate occurrence of an inflow venous congestion, the *decortication should never be performed beyond the coronary sulcus*. . . .

"Special attention must be given the apex of the heart which is usually firmly fixed and considerable difficulty is encountered in the attempts to liberate it. If decortication of the apex of the heart, which is bound down to the diaphragm, should not be successful, normal systolic contraction is impossible, because during inspiratory depression of the left dome of the diaphragm the heart is elongated and during systole becomes lancet shaped. In order to remedy this undesirable condition left-sided phrenicotomy is generally recommended, since this results in sufficient relief."

Graham in his book, "*Surgical Diseases of the Chest*" quotes Schmieden at length, and adds "It is not infrequently necessary to perform a Talma operation, since the operation of cardiolysis may take care of everything but ascites." A patient is presented in whom decortication failed to influence the ascites, and for whom a Talma operation was being considered when he died.

Churchill, who in 1928 operated successfully upon the first case in America, states:

"If the scar extends laterally over the left ventricle this region should be removed as the first step. Excision may be carried as far as the phrenic nerve, but I have in no instance sacrificed this structure.

"The sulcus formed by the descending branch of the left coronary artery is apt to be the site of densely adherent scar, and this region should be approached with caution to insure the preservation of this important vessel. In one instance a thickened calcified band 2 millimeters in diameter marked this sulcus. A maneuver that has been advantageous in several instances has been to establish a new plane of cleavage over the right ventricle so that the interventricular groove may be approached from both sides.

"A second very adherent region is the right auriculoventricular groove, in intimate association with the diaphragmatic pericardium. In many cases of the disease the mobilization of the auriculoventricular groove has been a crucial step in relieving the obstruction to right ventricular filling. Keith has shown that the free motion of the auriculoventricular groove is an important physiologic mechanism in the action of the right heart. Every effort, therefore, should be made to free this area if it can be done with safety, and once past it, the inferior cava can usually be readily exposed. Actual decortication of the auricle is a hazardous procedure owing to the thin wall of this chamber of the heart. It has been attempted in only 3 instances.

"Dissection of the diaphragmatic pericardium and scar from the heart should be as complete as possible but in no instance has it been carried to the left auricle. . . .

"When an area of encapsulated fluid exists it is important to resect the wall of the cavity that is in contact with the surface of the heart. The removal

of the parietal pericardium over such an area can be accomplished simply, but will not have the desired effect. A new line of cleavage must be established and a true decortication of the heart carried out."

Heuer and Stewart (18), who present an enviable record of 18 cases without a post-operative death, state:

"How much of the pericardium it is necessary to remove in order to achieve satisfactory results is a difficult question. We have removed as completely as possible the pericardium over the left and right ventricles, but have not attempted to remove the adherent pericardium over the auricles. An effort has been made to free the apex, and if possible the dissection is carried well down on the diaphragmatic portion of the pericardium. No attempt has been made to go beyond the right auriculoventricular groove; nor have we attempted to free the great vessels at the base."

Blalock and Burwell, whose review in 1941 is recommended for its excellent presentation of the pathologic, physiologic, clinical and surgical aspects of the disease, state:

"Most are agreed that actual decortication of the auricles is a hazardous procedure due to their thin walls and should not be attempted. If the ventricles are properly freed of scar, the undecorticated auricles are able to conduct sufficient blood to the ventricles to supply the needs of the body. . . . Several observers have commented on the need for the removal of the scar from the site at which the venae cavae enter the heart. It is our *impression that this is rarely necessary and even more rarely accomplished successfully*. . . . Schmieden states that complete liberation of the left ventricle is the most important part of the procedure and that in most cases this is the only surgical measure that is necessary. We question seriously the correctness of this view. Most patients with constrictive pericarditis have remarkably little dyspnea and edema of the lungs in comparison with the marked evidence of congestion in the systemic circulation. Most of the signs and symptoms are attributable to back pressure from the right side of the heart. In our experience, major emphasis has been devoted to decorticating the right ventricle. . . .

"An interesting unanswered question is concerned with the reason for the very slow improvement that occurs in many patients following pericardiectomy. The prevailing opinion is that the constriction has resulted in atrophy of the heart muscle and that a considerable time is required for a return to the normal condition. This explanation does not suffice in all instances. At any rate, *one should not despair if the improvement is slow and if a period of many months is required for the desired decline in the venous pressure* and the elevation in the cardiac output."

Harrington, in his report of 24 personally observed cases, states:

"I believe it is advisable to separate as much of the pericardial scar as possible from the ventricles, the right auricle and orifice of the inferior vena cava, and it is of particular importance to separate the attachment of the right ventricle to the diaphragm. It is of equal importance to separate the apex of the heart and I believe that this should be done early in the operation if possible. Separation of the heart muscle from its fixed attachments to the diaphragm is one of the most important considerations in re-establishing the action of the heart."

Beck, in discussing Harrington's article, states:

"The compression scar must be removed whenever it exists. Ventricles, auricles, venae cavae must be relieved of any compression in order to obtain a cure. Partial operations yield partial results and increase the probability of recurrence of scar."

Sellors, who presented in 1946 the latest review of the subject in the English literature, states:

"Excision should aim primarily and possibly only at freeing the ventricles, though for anatomical reasons even this is rarely achieved. The very thinness of the auricles and the great veins makes interference over them a hazardous undertaking. *At no time is it wise to carry dissection beyond the range of vision or unimpeded access*. . . . The obliquely placed auriculoventricular groove marks the upper limit, and though clearance beyond this area is frequently advocated it can be seen from a section of this region that there is little margin for error. . . . *It is highly doubtful that the constriction around the caval and auricular regions could ever produce such a degree of stenosis that a direct surgical attack on this region should be necessary*. . . .

"A lowering of the venous pressure and reduction of ascites and liver size may be noted within a few weeks, but full and final improvement should not be expected within 12 to 18 months. . . . The venous pressure often persists at a high level without causing the patient much inconvenience."

Decker, writing in 1947, argues that only the left ventricle requires decortication and that only a limited amount of pericardium should be removed as it is not an unnecessary organ!

The marked diversity of opinion expressed by these writers as to the extent of necessary decortication arrests one's attention. Striking also is their resigned acceptance of a long delay in securing improvement and reduction in

venous pressure following a presumed adequate pericardiectomy.

The purpose of this paper is to emphasize two all important principles in the operation for constrictive pericarditis: first, the necessity of exposing adequately the entire heart and its great vessels, so that the surgeon may have ready access to every strategic area requiring liberation, and, second, the imperative need of a wide removal of the diseased pericardium, not only that overlying the easily accessible anterior surface of the heart, but also that lying beyond or around each border of the heart, including most particularly the decortication of the right and inferior borders, and of the superior and inferior vena cava.

As to the operative approach for exposure of the heart, most of the above authors have employed the left parasternal incision with excision of segments of the third, fourth, fifth, and sixth ribs and removal of the left half of the sternum. One of the serious limitations of this approach is revealed in the following comment by Churchill:

> "For a time during the freeing of the adhesions about the vena cava, adequate exposure necessitated pressing on the right side of the heart with the flat surface of the hand. This distinctly interfered with the filling of the heart, and the anesthetist reported that the blood pressure could not be obtained."

Decker, in common with a few others, prefers the intrapleural approach through the left sixth interspace.

Both the left parasternal and the left transpleural incisions provide an unsatisfactory exposure of the right cardiac border, the liberation of which we believe to be the most essential part of the operation. Beck (3) realizing their inadequacy, has employed a bilateral approach through an H incision, but the intact midsternum limits greatly the necessary efforts of the surgeon. We should like to emphasize that the median sternotomy, from xiphisternum to second interspace provides an adequate and satisfactory approach. Some authors have recognized its value (Lilienthal, Roberts and Wilson), others state that its use is unnecessary, but we believe its merits will be increasingly appreciated. Having employed the usual left-sided parasternal approach in 2 patients, in which the right side was liberated with great difficulty, we then employed the median sternotomy in the next 7 patients, with extraordinary improvement in the ease and effectiveness with which the necessary decortication could be done.

As evidence that a more liberal decortication is necessary if delay in improvement or the persistence of a high venous pressure are to be avoided, we may cite the cases of secondary operations reported by several authors. Schmieden (30) recounts an instance in which he resected a "fünfmarkgrosses" fragment of pericardium (about 5 by 5 centimeters) which failed to correct the ascites and edema until a greater resection was performed.

In 2 of their 18 patients Heuer and Stewart (18) found it necessary to perform a second operation to free a greater part of the right heart. In 1 patient the second pericardiectomy was performed 5 years after the first operation, and in a second patient 8 years after the first operation. These authors also present some significant observations with reference to delayed improvement in their remaining patients:

> "In 7 patients improvement was evident at once or before the expiration of a month; improvement in 2 did not become pronounced until after the lapse of 2 or 3 months, in 5 not until after 6 to 10 months, and in 1 not until after 1 year. In 2, improvement was gradual, and in 3 improvement failed to occur. We have learned not to be discouraged if improvement after operation is not evident at once or rapidly."

Neuhof's experiences in 2 cases as presented by Friedberg and Hitzig are equally instructive. In Case 1 at the first operation in January, 1936, "a large portion of the pericardium overlying the right ventricle was removed," which, however, failed to correct the ascites, the pleural effusion, and the elevated venous pressure. In June, 1936, at a second operation the heart was approached through a left transpleural incision and a 7.5 by 5.5 centimeter fragment of pericardium was removed from over the left ventricle. Venous pressure remained elevated for 6 months but by December, 1936, it had dropped to 4 centimeters and the patient was well. In a second patient with ascites of a year's duration in whom a block of the inferior vena cava was postulated, the right side of the heart was

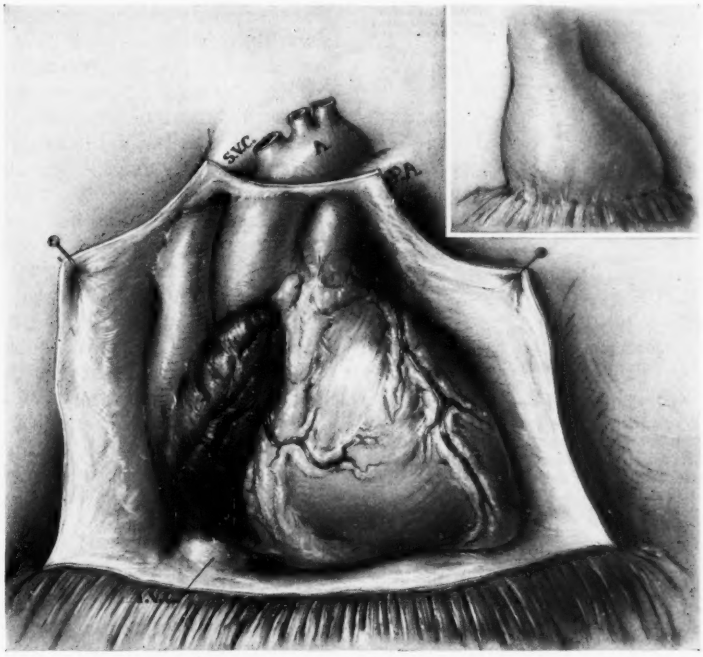

Fig. 1. Drawing from autopsy observation showing normal appearance of superior and inferior vena cava, indicating that both lie within the pericardium for 1 to 2 centimeters before entering the right auricle and are therefore subject to compression either by intrapericardial fluid or by contracture of pericardial scar or by the late calcium deposits in pericardial effusions.

freed through a right-sided approach at the first operation, which failed to correct the pleural effusion and the ascites. At the second operation 6 months later through a left transpleural approach, the pericardium over the left ventricle was excised. After this operation the ascites persisted temporarily, requiring 1 paracentesis, followed by complete recovery.

Harrison and White report 2 instances from Churchill's clinic in which reoperation was necessary. In 1 patient, ascites persisted for 2 years after the first operation but disappeared completely after a second pericardiectomy. In the second case, despite 2 pericardiectomies 14 months apart, and an omentopexy 4 months after the second decortication, the ascites was not corrected. At autopsy 6 years after the omentopexy it was seen that an area of the lower anterior portion of the pericardium measuring only 6 by 5 centimeters had been removed. There still remained over the left anterolateral aspect a calcified plaque 9 by 6 centimeters and over the anterolateral aspect of the right ventricle an area of pericardial calcification measuring 9 by 4 centimeters.

It may be categorically stated first, that a limited or incomplete removal of constricting scar may result in failure or long delay in the correction of ascites, and second, that when ascites does persist, not a Talma operation, but the removal of more scar is indicated. Failure to lower a high venous pressure may follow inadequate removal of scar overlying one of several areas: the right ventricle or auricle, the superior or inferior vena cava, or even the pulmonary artery at the base of the heart. Indeed, the pericardium over the left ventricle has not in any of our cases been as greatly thickened nor as "oppressive" as has

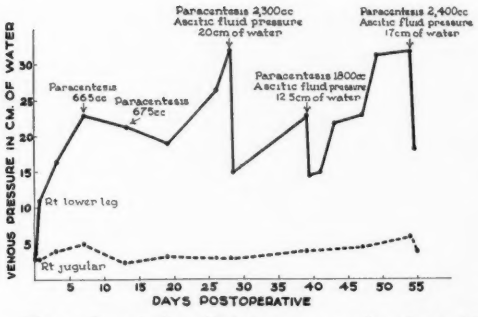

Fig. 2. Constriction of inferior vena cava in a dog to ½ its normal diameter produced a rise in venous pressure in the leg and a marked ascites noticeable on the 7th day. Note that the ascitic fluid reached a pressure as high as 20 centimeters of water, and that removal of the fluid reduced the venous pressure in the leg from 34 centimeters to 15 centimeters of water. A venous pressure of about 15 centimeters of water in the leg seemed to be the critical level at which ascites would develop.

the pericardium over the right heart and the 2 caval vessels. An explanation for this may lie in the greater and more forceful pulsating action of the left ventricle which forces the irritating pericardial fluid of the preconstrictive period into the less active and more quiet areas with consequently greater inflammatory excitation of the overlying pericardium. If the strongly pulsating, highly muscular left ventricle can be hampered visibly in its activity by a constricting pericardium as seen at fluoroscopy, how much more vulnerable to such constriction would be the easily compressible superior and inferior venae cavae as they lie in the intrapericardial space (Fig. 1). The effects of such compression have been studied in our experimental laboratory. Constriction of the inferior vena cava to one-half its normal caliber in a 14 kilogram dog produced a permanent ascites in approximately 7 days (Fig. 2). Constriction of the pulmonary artery to approximately one-half its normal caliber led to the development of an ascites in about 7 days (12). Constriction of the superior vena cava alone above the azygos vein produced no trouble, but when constricted below the entrance of the azygos vein, a pleural effusion occurred on about the ninth day (13). This last observation suggests that the pleural effusions so commonly observed in the presence of constrictive pericarditis may not be due necessarily to compression of the left heart but to superior vena caval constriction. Even more imperative, therefore, is the need of decorticating the superior vena cava.

The thickened pericardium lying between the inferior border of the heart and the diaphragm is also a critical structure requiring excision. Probably as the result of gravity, the irritating pericardial fluid, which precedes the scarring, is directed to the bottom of the pericardial sac, thus subjecting the diaphragmatic pericardium to the greatest inflammation, and therefore, to the greatest thickening and greatest subsequent contraction. This thickened pericardial sheet anchors the heart rigidly to the diaphragm, so that as the latter descends in inspiration, the heart is hampered even further by traction resulting in limitation of its filling and of its contraction. It is this increased restriction of cardiac filling and contraction during inspiration to which may be ascribed the momentary disappearance of the pulse, the so called paradoxical pulse, that invariably accompanies constrictive pericarditis.

The calcified and thickened pericardium on the posterior aspect of the heart cannot and need not be removed, but it is important to recognize that fibrous tissue will continue to contract; that the removal only of the easily accessible anterior pericardium is quite inadequate, and that a satisfactory pericardiectomy must include also excision of the constricting envelope beyond the left cardiac border, beyond the right cardiac border, and beyond the inferior cardiac border. This *beyond the border* decortication is necessary in order that the scar that remains may not, in contracting further, enclose the heart in its grip.

Our observations indicate also that there is considerable variation in the thickening of the pericardium, and therefore in the effects of its constriction, depending upon the part of the heart or great vessels involved. In Case 2, the patient had been troubled with ascites for 6 years which then spontaneously disappeared. There followed a puffiness of the entire face and head (Fig. 3) due to peripheral edema, which fluctuated with chemically induced diuresis. At operation, following decortication

Fig. 3. (Case 2). a, Insert shows puffiness of face 2 weeks before operation for constrictive pericarditis in which the superior vena cava was found markedly constricted. b, Two weeks after pericardiectomy the puffiness of face and peripheral edema had disappeared.

of the left and right ventricles, it was noted that both the inferior and superior venae cavae required liberation (Fig. 4), and that the superior vena cava above the heart no longer *bulged* after the removal of this critically located scar. It is very doubtful if venous pressure in the upper half of the body would have been altered in the slightest degree if the constricting pericardium around the superior vena cava had not been excised.

In Case 3, the patient's main complaints were varicose veins, bilateral varicocele, and progressive ascites (Fig. 5), all giving evidence of severe inferior vena cava obstruction. At operation the left ventricle showed fair expansile pulsation, the right ventricle was almost motionless under a thick layer of calcium infiltrated scar, and, as was anticipated, the inferior vena cava (Fig. 6) was found markedly constricted by calcified scar in direct continuation with the fibrotic and calcified pericardium

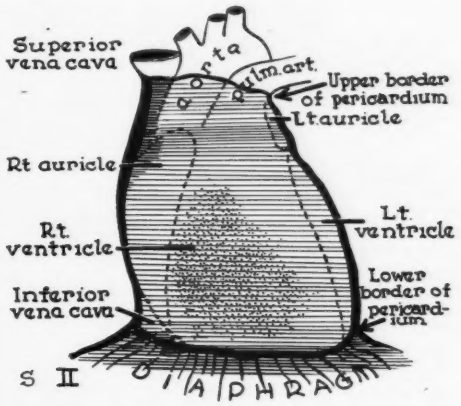

Fig. 4. (Case 2). Diagrammatic sketch of thickened pericardium found at operation around the superior vena cava which was greatly distended and bulged conspicuously above its entrance into the pericardial sac. The stippling indicates calcification found in the region of the right ventricle.

which securely anchored the heart along its inferior border to the diaphragm. Assuredly the ascites in this patient would not have been corrected if the inferior vena cava had not been effectively liberated.

In Case 4, also characterized by ascites, the entire heart was encircled by a thickened tuberculous pericardium, including a particularly heavy pericardiophrenic scar 1.5 centimeters thick extending horizontally across the inferior cardiac border, compressing the vena cava and mooring the heart tightly to the diaphragm (Fig. 7). The cure of this patient following an extensive pericardiectomy beyond each border of the heart has been spectacular and complete.

In Case 5, great improvement verging on normal health followed the evacuation of a pocket of tuberculous pus, and an extensive excision of greatly thickened pericardium. Its excision over the great vessels at the base of the heart was followed immediately by visible improvement in the vigor of cardiac contraction, which was even more visibly improved by the freeing of the 2 venae cavae (Fig. 8).

The best evidence of an adequate pericardiectomy is a prompt and permanent reduction in the venous pressure (Fig. 9). In 3 of our patients, differences in the venous pres-

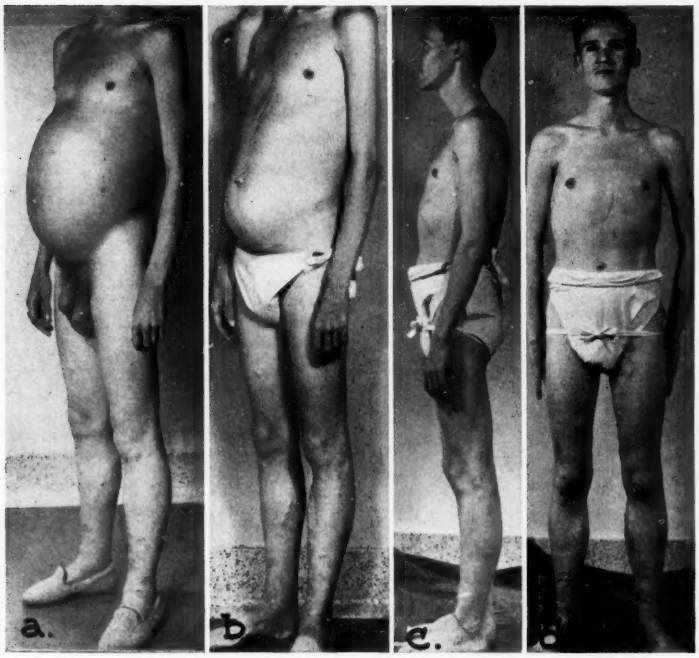

Fig. 5. (Case 3). a, Marked ascites, bilateral varicocele, and bilateral varicose veins in presence of constrictive pericarditis. b, Prompt improvement within 3 weeks after operation performed on July 7, 1947, which disclosed a marked constriction of the inferior vena cava. c, d, Complete cure October 24, 1947.

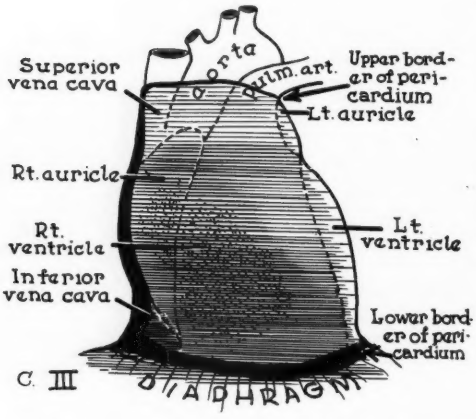

Fig. 6. (Case 3). Diagrammatic sketch of operative findings showing very mildly thickened pericardium over the left heart, marked thickening and calcification over the right heart and inferior vena cava, and along the inferior cardiac border fixing the heart rigidly to the diaphragm.

sure of arm and leg were recorded before operation. These differences were undoubtedly related to the associated ascites, the result probably of inferior vena cava compression. A somewhat high residual venous pressure in Case 5 is attributed to our inability to remove calcified tuberculous scar penetrating the cardiac musculature. In some instances the long delay but ultimate lowering of venous pressure in the arm may conceivably be due to impeded flow of blood through the superior vena cava resulting from its incomplete decortication. If by chance the inferior vena cava in such a patient had been adequately liberated, the unimpeded flow of blood through it would, during succeeding months, encourage the development of a collateral venous bed by way of this unconstricted vessel which would be accompanied *pari passu* by a reduction of the venous pressure present in the arm.

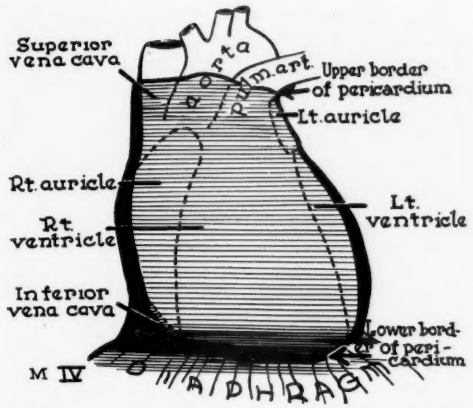

Fig. 7. (Case 4). Diagrammatic presentation of operative findings showing marked thickening of entire pericardium without calcification, with particular thickening of the pericardium between the heart and the diaphragm, compressing the inferior vena cava and producing ascites, which disappeared promptly following pericardiectomy.

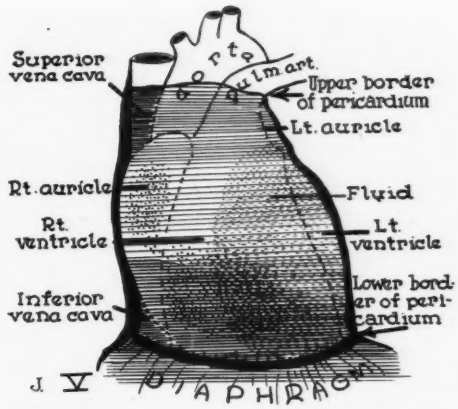

Fig. 8. (Case 5). Diagrammatic sketch of operative findings showing thickened pericardium, particularly across the base of the heart. A pocket of intrapericardial tuberculous pus lay over the anterior heart surface. Stippling shows areas of calcification which penetrated the cardiac musculature.

It may be true, as Blalock and Burwell contend, that compression of the right heart is usually responsible for most symptoms, but we would add that constriction of the vena cava may continue to be a disappointing source of trouble if only the right heart is decorticated and actual liberation of the venae cavae is disregarded.

That late improvement may occur even after a limited pericardiectomy is patent. A possible explanation is that the heart through more vigorous pulsation may slowly extrude

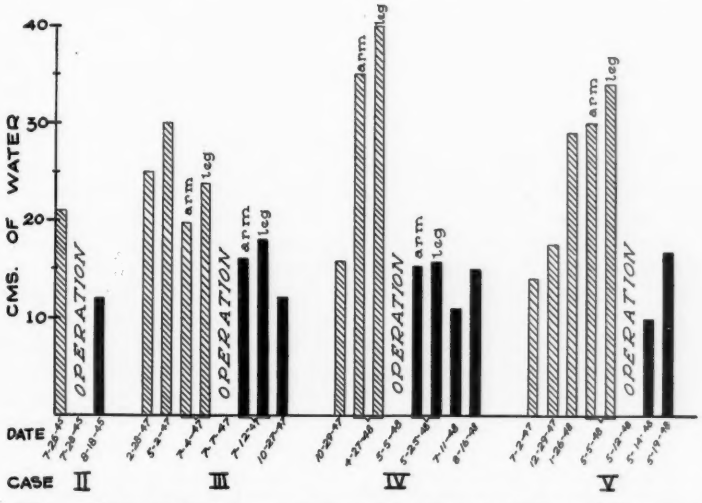

Fig. 9. Marked reduction in venous pressures as determined before and after operation. Note preoperative differences in pressure in arm and leg in last 3 cases, probably explicable on basis of an associated ascites.

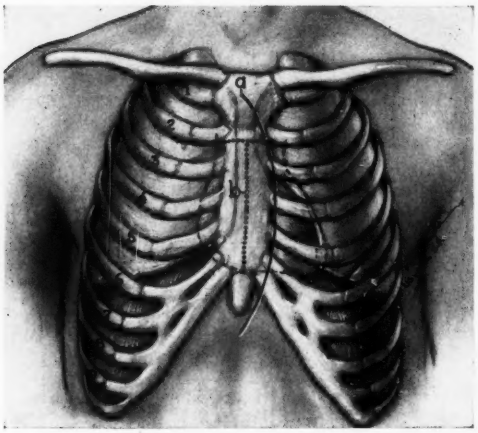

Fig. 10. Steps in pericardiectomy: *a*, Incision in skin is excentrically placed to avoid its lying directly over vertical incision, *b*, through midsternum. Xiphisternum is excised. Sternum is divided horizontally in 2d interspace.

itself from its investing pericardium, or that gradual and slow recession of the scar left around the heart results in decompressing critical areas.

Profiting by the experiences and suggestions of the surgeons quoted earlier in this paper (3, 5, 6, 8, 11, 14, 15, 18, 19, 20, 24, 28, 31, 32) and by our own observations in 9 clinical cases, confirmed by experiences in the experimental laboratory, the following plan of operative procedure is presented (Figs. 10 to 18).

TECHNIQUE

A median sternotomy is performed, with excision of the xiphisternum and horizontal division of the sternum in the second interspace. The use of the power saw in dividing the sternum or of the powerful long-handled Bethune bone-cutting forceps is to be preferred to the Lebsche "sternal knife" or chisel which necessitates pounding upon the chisel and indirectly upon the bone with a mallet. The latter technique must be condemned for its shocking effect upon an already seriously ill patient. It was noted in the old days of operations for now almost extinct chronic osteomyelitis that the hammer and chisel were lethal weapons to be avoided by surgeons in very ill patients.

The objection that in median sternotomy both thoracic cavities may be entered is no longer valid since intratracheal anesthesia is usually employed. A rent into the left pleural cavity can usually be avoided or can be closed successfully, but it is almost inevitable that the right thoracic cavity be entered if adequate liberation of the vena cava is to be achieved. Following careful displacement of the pleura lateralward on both sides, the pericardium is incised over the area of the left ventricle, and is cautiously mobilized beyond the left border of the heart as far laterally as the left phrenic nerve if it can be identified, but which should not be injured; the pericardium over the right ventricle is then mobilized anteriorly, with excision of the pericardium overlying the pulmonary artery, the ascending aorta, and the superior vena cava. The right border of the heart is freed so as to yield a good view of the superior and inferior venae cavae. Inferiorly, the heavy, frequently calcified pericardium lying between the inferior border of the heart and the diaphragm is then excised from the inferior vena cava on the right border to the apex of the left ventricle on the left border. In this excision normal bundles of the diaphragm should be exposed.

The right auricle must be liberated with caution if direct removal of the overlying pericardium is attempted. That its removal is possible was proved by our experiences, but if this seems too hazardous, the pericardium may be incised, both along the auriculoventricular groove, and at the base of the heart, leaving the intervening pericardium attached to the auricle. This maneuver has the effect of liberation and should permit the desired expansion of the auricle.

The closure of the median sternotomy is easily effected by the use of 2 or 3 No. 20 stainless steel sutures applied not to cartilage but to the bony part of the sternum, a precaution designed to avert infection in such poorly vascularized tissue as cartilage.

We consider removal of the thoracic wall overlying the heart as unnecessary. In constrictive pericarditis the heart is limited not by the bony thorax but by the pericardium. In Case 2 the sternum and ribs have completely

Fig. 11. The 2 halves of sternum are separated by self retaining rib spreader applied after freeing mediastinal areolar tissue and right and left pleurae from undersurface of sternum and rib cage.

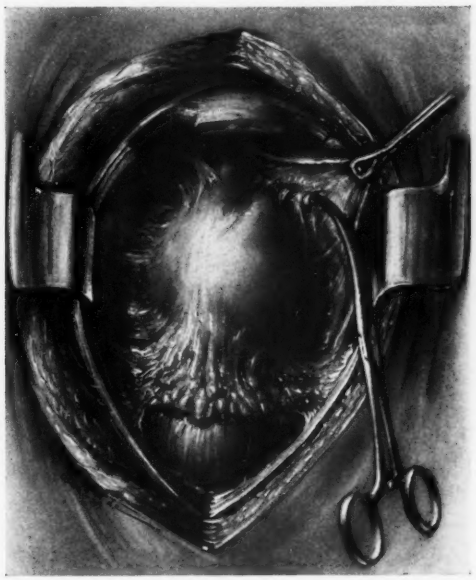

Fig. 12. Pleura and lung are dissected free from anterolateral pericardium on both sides to permit excision of thickened pericardium as far, approximately, as the phrenic nerve, which however is not easily or always indentifiable.

regenerated and the patient remains perfectly well. In Case 4 roentgenograms taken since the median sternotomy was performed show a marked shift of the heart when the patient's position is changed from one side to the other indicating that it has not become rigidly fixed to the undersurface of the replaced sternum.

Because of the large area of denuded and traumatized tissue produced by pericardiectomy, sometimes performed in the presence of active tuberculous granulation tissue, there may be a considerable outpouring of wound fluid necessitating drainage of the operative site. This drainage has been effected by deliberately incising the right pleura along its mediastinal border where it has not already been opened and providing for removal of the fluid from the right chest either by repeated aspirations (Case 3) or by intercostal tube drainage (Cases 4 and 5). In the 3 cases in which median sternotomy was used, complete primary healing of the operative wound has occurred—even in the presence of an active tuberculous pericarditis as in Cases 4 and 5.

That such drainage from the large operative area is necessary is evident from our experiences. In Case 3 following operation on July 5, the right chest was aspirated 4 times in the period from July 7 to August 14 for a total of 1970 cubic centimeters of bloody fluid. In Case 4 only 100 cubic centimeters of serosanguineous fluid escaped from the intercostal catheter in the first 24 hours, and none thereafter, but on the second postoperative day 280 cubic centimeters of reddish fluid was aspirated from the right chest and none thereafter. In Case 5, 1,100 cubic centimeters of serosanguineous fluid escaped from the intercostal drainage tube in the first 24 hours, 400 cubic centimeters in the second 24 hours, and none thereafter. Several aspirations were performed subsequently with gradual reduction in the amount of fluid removed. Most writers do not advocate drainage of the wound, but it is instructive to note that in 15 of Heuer's 18 cases, none of which was drained, an accumulation of fluid occurred in the chest, for which aspiration was found necessary in 7 cases.

Fig. 13.

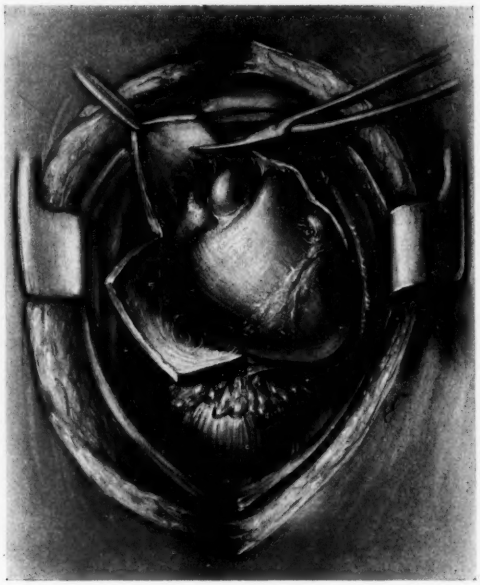

Fig. 14.

Fig. 15.

Fig. 13. Incision is made in pericardium over the presumed site of the left ventricle and the left border and apex are dissected free first.

Fig. 14. Anterior surface and base of heart are completely freed, if calcification permits, with excision of pericardium over pulmonary artery, aorta, and superior vena cava.

Fig. 15. Right anterolateral border of heart is liberated by excision of pericardium overlying right auricle and inferior vena cava. Right pleural cavity is usually entered during this dissection. Right phrenic nerve should not be injured.

A useful tool in separating the heart from the pericardium is the so called "peanut" dissector, a small round pea-sized bit of gauze in a curved clamp. By painstaking slow dissection, now blunt, now sharp, the proper cleavage plane can be maintained, but is easily lost

Fig. 16.

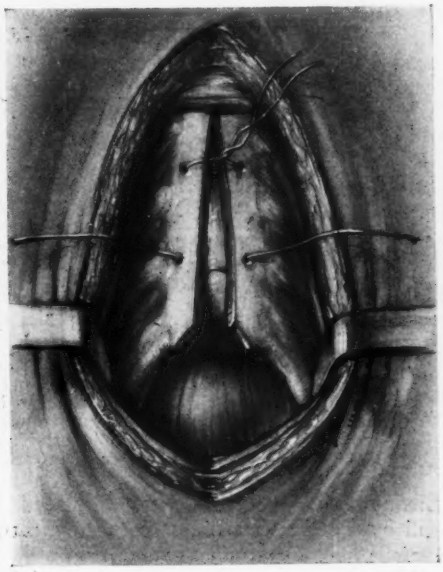

Fig. 17.

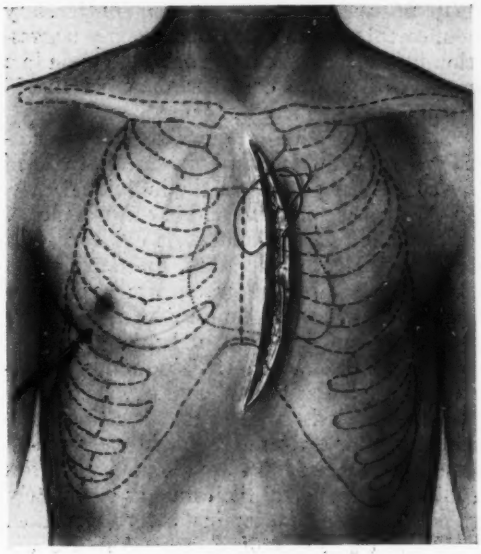

Fig. 18.

Fig. 16. Decortication is completed by excision of pericardium, usually greatly thickened and calcified, lying between anteroinferior border of heart and the diaphragm. Normal muscle fibers of diaphragm may be brought to view during this dissection, which should run from inferior vena cava to apex of heart.

Fig. 17. Sternum is reapproximated by 2 heavy steel wires placed in bony part of sternum—not in avascular cartilaginous part.

Fig. 18. Fascia and deep subcutaneous tissue are reapproximated with interrupted silk or cotton sutures and skin is reapproximated with fine steel or silk sutures. Right pleural cavity may be deliberately connected with mediastinal space and drained by intercostal catheter in 5th or 6th interspace in nipple line.

if speed is the watchword rather than safety. Bigger's suggestion to retain the pericardium back of the advancing edge of dissection between pericardium and myocardium may be lifesaving in case the myocardium wall is accidentally perforated, or excessive bleeding is

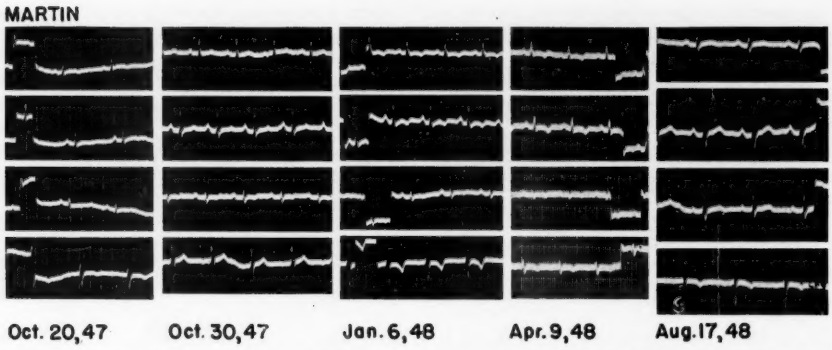

Fig. 19. Case 4. October 20, electrocardiogram in the presence of a pericardial effusion showed low voltage in the *QRS* complex, and inverted T_1 and T_4 and flat T_2 and T_3. October 30, normal electrocardiogram with increased *QRS* voltage, and upright *T* waves accompanied the subsidence of effusion and reduction in cardiac shadow. January 6 to April 9, the development of cardiac constriction was accompanied by decreased *QRS* voltage and by inverted *T* waves. August 17, pericardiectomy May 12 was followed by marked improvement in *QRS* voltage and by normal upright *T* waves in leads *1*, *2*, and *3*.

encountered. Resuturing the liberated but still attached pericardium to the myocardial surface may be an effective control.

Klose's suggestion that the pericardial defect be repaired with a fat or fascial transplant may be cast into the limbo of unnecessary refinements as may also Beck's early suggestion that these patients be operated upon in a negative pressure chamber to avoid the ill effects of pneumocardiac tamponade.

Selection of the optimum time for operation may be difficult, and must be determined by conditions present in the individual case. In the absence of fever, and in the presence of calcification, which in itself is evidence of a long standing chronic state, the detrimental effects of the disease are wholly mechanical in origin and the operation may be done at any time following a period of bed rest, during which the elimination of tissue fluids is promoted by a low sodium diet and by chemically induced diuresis. Optimum nutrition with supplementary vitamins should be stressed and the thoracic and abdominal cavities should be emptied of their fluid as completely as possible by aspiration just before operation.

When the signs of compression are accompanied also by signs of acute inflammation, the problem becomes twofold: control of infection, and correction of the mechanical obstruction to the normal circulation of the blood. The immediate treatment of the infection obviously requires rest in bed, optimum nutrition including supplementary vitamins, the administration of penicillin and streptomycin on the assumption of tuberculosis since tuberculosis usually cannot be proved or disproved until operation, and the correction of anemia. Improvement will be apparent from the reduction in fever, lowering of pulse rate and decreased sedimentation rate. Operation may be delayed until such improvement is manifested, but should not be delayed long if the mechanical disturbances of compression are prominent, incapacitating, and progressive. Under these conditions, the sooner the compression is corrected the better will be the ultimate results. In Case 4 only 7 months elapsed from the onset of symptoms due to acute pericarditis with effusion to pericardiectomy for constricting pericardium; in Case 5, 10½ months elapsed. In both cases tubercle bacilli were demonstrated on culture of pericardial fluid removed at operation.

The administration of streptomycin decreases the hazard of operating in the presence of active tuberculous pericarditis, as these cases illustrate. In Case 4, streptomycin was reserved for the immediate postoperative period, since this was considered the crucial period of recovery, and its administration was continued for 3 months after the operation.

In Case 5, on the assumption of an active tuberculous pericarditis, streptomycin, 1 gram

daily, was administered from November 27, 1947, to March 23, 1948. Pericardiectomy was performed May 15, 1948, and streptomycin, 2 grams daily, was again administered from May 10 to July 6, and 1 gram daily from July 6 to August 10, 1948.

The problem of early diagnosis, and the recognition of the disease, have been greatly clarified in the writings of White, Levine, Beck (1, 2), Burwell, and others. As Levine states, "it is amongst patients who are regarded as having heart failure, but in whom the ordinary causes are lacking, i.e., hypertension, coronary sclerosis, valvular disease, hyperthyroidism, or who are thought to have cirrhosis of the liver, in whom constrictive pericarditis will be found." Moreover, it is more commonly found in younger patients, the average age of 100 reported cases being only 25 years.

Any young patient, therefore, who presents symptoms suggestive of myocardial failure, but who has ascites or pleural effusion or peripheral edema associated with heart sounds that are quiet or muffled, and unaccompanied by a murmur, whose cardiac borders move but little under fluoroscopy, whose arterial pressure is low and pulse pressure small, and whose venous pressure is above 15 centimeters of water in the arm and 5 centimeters to 10 centimeters higher in the leg, should be strongly suspected of having constrictive pericarditis, and should be surveyed again with this diagnosis in mind. Particularly suspect should be the patient who has Beck's triad of a "small, quiet heart, ascites, and increased venous pressure," associated with the corroborative evidence of an electrocardiogram exhibiting low voltage in the *QRS* complex and inversion of the *T* waves (Fig. 19).

SUMMARY

In 265 recorded operations for constrictive pericarditis, 22 deaths occurred on the operating table, 48 deaths occurred in the early postoperative period, 118 cases were considered cured and 44 cases improved.

The following important factors contributed to the success of the operation: its application in young individuals in whom other organs were normal and in whom liberation of the compressed heart or its vessels was the only correction necessary; the availability of intratracheal anesthesia, and of oxygen, transfusions and antibiotics; an adequate exposure of the heart permitting ready access to critical areas for the removal of the offending scar; the courage and technical skill of the operating surgeon which enabled him to pursue the operation until adequate decompression of all critical areas had been achieved.

Factors contributing to poor results were such considerations as the etiology of the primary pericarditis, whether tuberculous or pyogenic; the selection for operation of exceedingly ill patients; technical difficulties such as tears in the thin-walled auricle or in the myocardium of the right ventricle; inability to remove the scar because of penetration of cardiac musculature by calcium deposits; failure to remove scar over critical areas such as the inferior and superior vena cava; technical difficulties imposed by inadequate exposure of the heart; and lastly, the postponement of a correct diagnosis until the liberation of attenuated and atrophied myocardium resulted only in circulatory failure.

A satisfactory and adequate pericardiectomy must include liberation of all borders of the heart, and of both venae cavae. The inferior cardiac border must be liberated by excision of the pericardium lying between the heart and the diaphragm.

Persistence of ascites following pericardiectomy is evidence of an inadequate decortication and demands reoperation and removal of more scar, rather than an omentopexy or Talma operation.

The best evidence of an adequate operation is prompt and permanent lowering of venous pressure.

To achieve the exposure necessary for an adequate inspection and decortication of the heart, a median sternotomy with transverse division of the sternum in the second interspace is recommended. Reapproximation is by several stainless steel sutures inserted through bone, not through avascular cartilage.

The wound should be drained, preferably into the right pleural space from which the fluid can be removed either by aspiration or by intercostal drainage.

In cases suspected of having tuberculosis or in which evidence of active inflammation is present, the preoperative preparation should include a prolonged period of bed rest with optimum nutrition, and the administration of penicillin and streptomycin. Operation should not, however, be deferred unduly, if the symptoms of compression are incapacitating, unaffected by therapy, and progressive.

Nine patients have been operated upon: 5 of unknown etiology, with 1 dead, 3 cured, 1 improved; and 4 of active tuberculous pericarditis, with 2 cured, 1 markedly improved, 1 improved.

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BRONCHIECTASIS

A Study of the Segmental Distribution of the Pathologic Lesions

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WITHIN recent years, interest has been manifested in the possibility of resecting lung segments in bronchiectasis as opposed to performing lobectomies. The principles underlying the procedure of segmental lung resection are several.

The first and most important assumption is that bronchiectasis is not a progressive disease, or at least that the disease has progressed as far as it will by the time diagnosis is made (1), and thus that extension from one segment to another is not by spread of the bronchiectatic process from the affected segment but by involvement of the unaffected segment by an acute pulmonary infection. Such a view, of course, may be colored by an individual's underlying concept of the disease. It is an open question at the present time whether bronchial ectasia (from which the disease is named) is a primary phenomenon or merely secondary to parenchymatous disease. Certainly, it seems reasonable to suppose that an infected segment could, by overflow into another suitably situated segmental bronchus, produce infection of that segment (2). In reviewing his cases of segmental resection, Pilcher states, "It appears on review of these cases that in some the interval between bronchogram and operation has been too long, and there may have developed in the interval areas of disease which were not present before."

The second assumption is based on the consideration that bronchiectasis is primarily a segmental disease (1, 3, 7), even though it is very frequently multilobar (80 per cent in Churchill's series). We have seen no detailed pathologic study to confirm this, though in a general way it appears to be correct; for example, the lingular segment of the left upper lobe is usually the only segment of this lobe involved.

The third consideration involved is the obvious advantage of preserving as much healthy lung tissue as possible for the patient's benefit, especially in bilateral and extensive disease. There is, of course, no criticism of this thought.

If these assumptions are correct, there should be no histopathologic changes present in segments which are normal bronchographically and grossly. Therefore, such segments may be saved for the patient's benefit.

With these points in mind, we thought it worthwhile to make a pathologic study of bronchiectatic lung tissue by examining each segment in detail. Only 7 cases have been studied over a 6 month period but it was thought that a report of even a limited study might emphasize the importance of detailed examination of the lungs in a problem which is still controversial.

The material consists of 7 cases of fairly early bronchiectasis in children, for which lobectomy, and in 1 case pneumonectomy, was performed by Dr. Dudley E. Ross. As lingulectomy was the only form of segmental resection used, it was possible for us to study the gross and microscopic lesions in a number of segments, some of which were normal roentgenographically and some of which were diseased.

Examination of the lungs was carried out as soon as the specimens were brought from the operating room. They were dissected segmentally. The nomenclature is that used by Foster-Carter. Careful observations were made on the gross specimens, both before and after fixation of the specimen in 10 per cent formol saline. Depending on the size of the lung, one, two, or three sections were taken from each segment for histological examination. These were stained by modifications of Masson's trichrome technique, Weigert's stain

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TABLE I

Case No.	Age years	Sex	Symptoms	Duration of symptoms	Illnesses prior to onset of symptoms	Illnesses after onset of symptoms
1	11	F.	Cough, nonproductive; intermittent fever	8 yrs.	Repeated u.r.i.; bilateral bronchopneumonia; acute otitis media (right)	9 hospital admissions for pneumonia; whooping cough (1 yr.); measles (2 yrs.)
2	3	M.	Cough, no mention of sputum; intermittent fever	2 yrs. 1 mo.	Bronchopneumonia; nephritis	
3	8	F.	Cough, moderate amount of sputum	5 yrs.	Bilateral pneumonia	Frequent "colds"; continuous nasal discharge; whooping cough; measles, chicken pox, mumps
4	2	M.	Cough with considerable greenish sputum; anorexia; failure to grow; pallor	1 yr.	Measles; pneumonia	Frequent "colds"
5	10	F.	Cough, mod. productive; frequent fever; nasal discharge	3 mos., 3 mos. 3 mos.	Pneumonia; chronic pansinusitis; chicken pox; measles; whooping cough; bronchopneumonia	
6	9	F.	Cough, productive	6 yrs.	Bronchitis; mumps	Measles; whooping cough
7	9	F.	Cough, no mention of sputum; failure to gain weight; anorexia	Since infancy		Chronic bronchitis; polio (bulbar palsy) 1946

for the elastic tissue, and hematoxylin and eosin.

GENERAL DESCRIPTION OF THE CASES

The patients, of whom 2 were males and the remainder females, varied in age from 2 to 11 years. The symptoms dated from 1 to 8 years prior to the operation. Further details are given in Table I.

Lipiodol installation was the most important diagnostic procedure used to determine the presence and distribution of bronchiectasis and was carried out in all cases (Table II). The roentgenographic distribution of the lesions is clearly indicated in Table II. The implications will be discussed later. Except in 2 instances (i.e. Case 5, in which pus was seen in the bronchus to the posterior basic segment and Case 4 in which all segments of the right side were involved) bronchoscopic examinations were not helpful in the localization of the disease according to segments.

GROSS APPEARANCE OF SPECIMENS

The lung parenchyma in all cases presented a uniform type of change. It was moderately collapsed and soft to doughy on palpation. Aeration was minimal and the cut surface was jelly-like to gelatinous as seen under the hand lens. No gross scarring was seen. There was no striking difference in the parenchyma between involved and uninvolved segments. In Case 4, the major bronchi were nodular.

In Cases 1, 2, and 3 no bronchial ectasia and only questionable bronchial wall thickening were noted. Gross changes of the bronchi in the dorsal segment in Case 4 were present, while in Case 7 there was slight ectasia without thickening. In the remainder of the cases no gross lesion was apparent in the dorsal segment bronchi. In Case 5 the lingular bronchi showed slight thickening of the wall, while the basilar bronchi showed moderate changes of the same type. The lingular bronchi in Case 7 showed somewhat more marked changes than the basic segments. In Case 6 the middle lobe bronchi showed somewhat more marked gross changes than the basic.

The distribution of bronchial contents did not always correspond to the degree of ectasia. Except in Case 4, the bronchial contents were more mucoid than purulent and were relatively scanty.

HISTOPATHOLOGY

Before dealing in some detail with the lesions of the segments which on bronchographic and gross examination were uninvolved, a consideration of the overall picture in these cases will be made. The essential lesions were inflammatory in nature with the lymphocyte and monocyte as the predominating cells but a few neutrophils were present as well. The cellular infiltrate and fibrosis varied considerably from case to case and segment to segment. The bronchial inflam-

TABLE II.—BRONCHIECTATIC INVOLVEMENT

Case No.	Bronchographic findings		Microscopic degree of involvement				Musculoelastic lesions	Extent of operation
			Segments	Lobe	Inflammatory	Fibrosis		
1 199	A.B.	Mild	D.	Lower	+	+	o	Right lower lobe
			A.B.		++	+	o	
			M.B.		++	o	o	
			P.B.		++	o	o	
2 224	D.	Not filled	D.	Lower	+++	++	o	Right lower lobe
	A.B.	Minimal	A.B.		++++	++++	+	
	M.B.		M.B.		++++	++++	+	
	P.B.		P.B.		++++	++++	+	
3 235	A.M.	? No dilatation	A.M.	Lower	++	+	o	Left lower lobe and lingula
	L.M.	? No dilatation	L.M.		++	+	o	
	A.B.	Very minimal	D.		++	++	o	
			A.B.		+++	++	o	
	M.B.		M.B.		++++	+++	o	
	P.B.		P.B.		++++	o	o	
4 253	A.	Quite marked (Cylindrical and saccular)	A.	Upper	+	o	o	Pneumonectomy right
	P.L.		P.L.		++	+	o	
	A.L.		A.L.		+++	++	+	
	A.M.		A.M.	Middle	+++	+++	+	
	L.M.		L.M.		+++	+++	+	
	D.		D.	Lower	++++	+++	++	
	A.B.		A.B.		++++	+++	++	
	M.B.		M.B.		++++	+++	++	
	P.B.		P.B.		++++	+++	++	
5 254	A.M.	Slight	A.M.	Lingula	+++	++	+	Left lower lobe and lingula
	L.M.		L.M.		+++	++	+	
	A.B.	Moderate	D.	Lower	++	+	o	
			A.B.		++++	++	+	
	M.B.		M.B.		++++	+++	++	
	P.B.		P.B.		++++	+++	++	
6 281	A.M.	Slight	A.M.	Lingula	++++	+++	++	Right lower and middle lobes
	L.M.		L.M.		++++	+++	++	
	A.B.	Minimal	D.	Lower	+	o	o	
			A.B.		++	++	o	
	M.B.		M.B.		++	++	o	
	P.B.		P.B.		+++	++	+	
7 298	A.M.	Moderate	A.M.	Lingula	++	++	o	Left lower lobe and lingula
	L.M.		L.M.		++++	++	++	
	D.	Moderate	D.	Lower	+	+	o	
	A.B.		A.B.		+++	+	o	
	M.B.		M.B.		+++	++	o	
	P.B.		P.B.		+++	++	o	

+, Very slight; ++, slight; +++, moderate; ++++, marked
A., Apical; A.L., anterolateral; L.M., lateral middle; A.B., anterior basic; P.B., posterior basic; P.L., posterolateral; A.M., anterior middle; D., dorsal; M.B., middle basic.

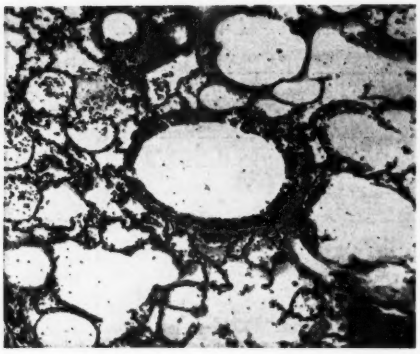

Fig. 1. Photomicrograph of a normal bronchiole and adjoining alveoli of a 9½ year old child. For comparison with the other photomicrographs presented in this contribution. ×65.

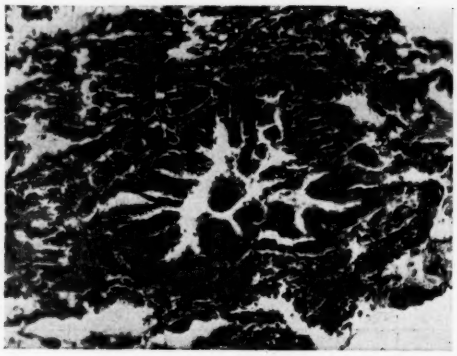

Fig. 2. Photomicrograph of dorsal segment bronchiole in Case 1. Small subepithelial granulation tissue mass in right upper area of bronchiole. Focal adventitial inflammatory infiltrate. Segment normal bronchographically. ×135.

matory lesions in our opinion became more and more marked as the bronchi became smaller. The major bronchi showed lesions which were not so severe as were those in the small bronchi and the bronchioles. Scarring also was more marked peripherally than centrally.

Lesions of the parenchyma (including respiratory or transitional bronchioles and alveoli) were common. The alveolar lesions were often focal and seemed to be related to involved respiratory and terminal bronchioles, as well as to small bronchi. The lesions were those of inflammation with scarring. Probably alveolar fibrosis predominated over interstitial alveolar wall inflammation. Alveolar exudates were uncommon over a large area but occasional foci involving several alveolar lumens were found (except in Cases 1, 4 and 7). Traces of previous alveolar inflammation, as indicated by fibrous polyps occupying the lumens, were found in Cases 2, 3, and 5. Tiny subepithelial fibrous or granulation tissue masses were found projecting into the lumens

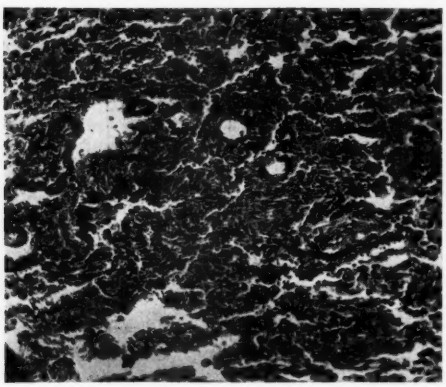

Fig. 3. Photomicrograph of respiratory bronchiole of left anterior middle segment in Case 3. Just above the center of the field is a tiny lymphatic surrounded by a collar of lymphocytes and neutrophils. A similar infiltrate is present in the alveolar wall in the lower right hand corner, as well as an area just above it. Bronchographically, there was no dilatation demonstrable in either of the lingular segments. ×125.

Fig. 4. Photomicrograph of dorsal segment bronchiole in Case 2. There is moderate subepithelial fibrosis. Note muscle fibers at lower right hand corner of bronchiole. There is alveolar fibrosis below the bronchiole. Segment not filled bronchographically. ×50.

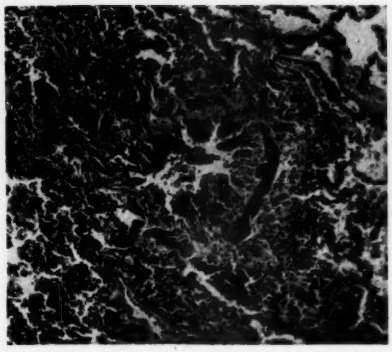

Fig. 5. Photomicrograph of dorsal segment bronchiole in Case 3. Slight diffuse adventitial inflammatory infiltrate. At bottom of photograph, note the exudate lying in the tissues parallel to a small lymphatic vessel. Segment normal bronchographically. ×125.

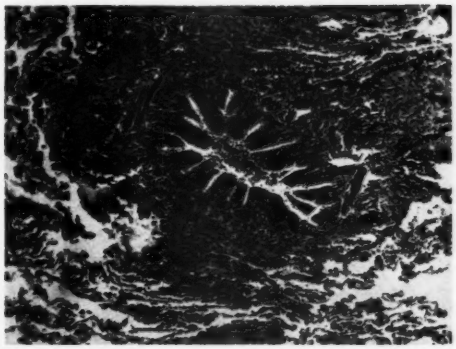

Fig. 7. Photomicrograph of small dorsal segment bronchus in Case 5. Moderate adventitial inflammatory infiltrate and fibrosis. At the bottom of photograph, note the irregular scar extending into the parenchyma. Segment normal bronchographically. ×65.

of the terminal and respiratory bronchioles in all cases. Partially collapsed alveoli were prominent.

Mucosal ulceration was rare and when present was focal in character. The epithelium was essentially normal with normal cilia in all cases, except Case 4, where a slight degree of focal metaplasia existed. Destruction of the elastic and muscle coats was far from striking, as can be seen from Table II, and was mainly focal in character. There was no correlation between ectasia, as demonstrated by bronchogram, and loss of these coats. In all instances, except those segments showing marked inflammation, normal bronchi and bronchioles existed side by side with involved tubes. As the blocks were not serial sectioned, it is difficult to say whether such normal bronchi were uninvolved in their entire length. Focal and diffuse scars were found in some, either in the submucosa, the adventitia, or both.

Lymph follicle formation in the bronchial walls was not as marked a feature in most of these cases, as compared to the number present in well marked chronic bronchiectasis. Endarteritis obliterans of the pulmonary arteries was present only in those segments which

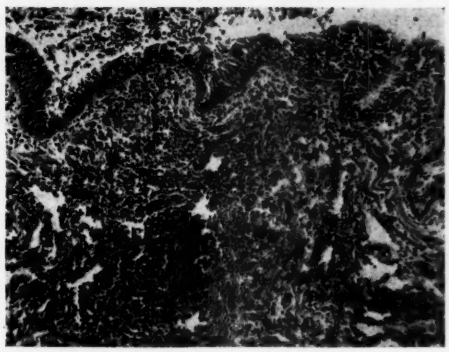

Fig. 6. Photomicrograph of dorsal segment bronchus in Case 4. Marked inflammatory lesions with slight fibrosis. Quite marked ectasia is demonstrated bronchographically. ×65.

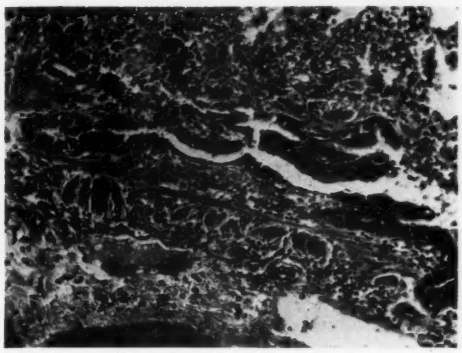

Fig. 8. Photomicrograph of dorsal segment bronchiole in Case 6. This shows a slight inflammatory infiltrate of the submucosa and adventitia. Segment normal bronchographically. ×125.

Fig. 9. Photomicrograph of small dorsal segment bronchus in Case 7. This segment showed very slight microscopic lesions, yet bronchographically there was moderate ectasia. Here there is seen a very slight peribronchiolar invasion by inflammatory cells. ×65.

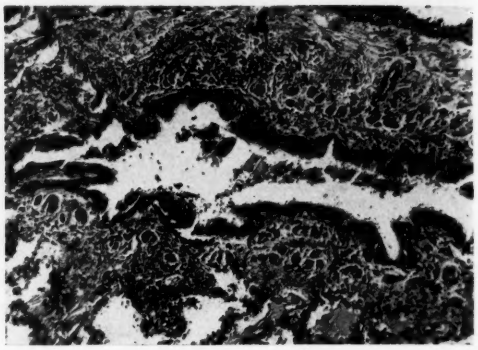

Fig. 10. Photomicrograph of small bronchus of mid basic segment in Case 1. Moderate inflammatory exudate of submucosa and adventitia similar in degree to the roentgenographically dilated anterior basic bronchi. Segment normal bronchographically. ×65.

were severely involved and was not a marked feature.

The lesions of the segments which were uninvolved on bronchographic and gross examination were on the whole similar in type but quantitatively less. These lesions are of the greatest interest in view of the inference in the surgical literature on segmental resection that bronchographically normal segments, found to be grossly normal at operation, can be safely left behind. Such seem to apply in the main to the dorsal segment of the lower lobes as it is admitted that in nearly all cases the three basic segments and the lingular segments are usually involved. Churchill and Belsey do state, however, that commonly only the posteromedial (anterior middle branch in our terminology as far as could be determined) branch of the lingula is involved and it is a rare occurrence for both of the segments to be diseased.

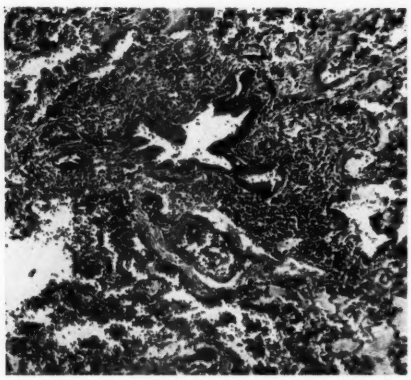

Fig. 11. Photomicrograph of bronchiole in posterior basic segment in Case 1. Moderate inflammatory exudate involving whole thickness of wall with slight fibrosis. This was equal in degree to that of the anterior basic segment which alone was dilated bronchographically. ×65.

In these 7 cases the microscopic involvement varied somewhat in different cases but in none of the supposedly normal segments were the lesions marked. In those noted as "very slight" in the table, the lesions were focal and were minimal in degree. They are perhaps colored by individual interpretation, nevertheless, we consider that such lesions are not present in normal lungs at this age. Those cases marked as "slight" in the table were minimal in degree but were fairly diffusely scattered throughout the segment and there is no doubt that these changes are abnormal.

The lesions were those of inflammation and its sequelae. The bronchial lesions consisted of thin infiltrations of lymphocytes with occasional neutrophils in the submucosa or adventitia. These tended to be focal rather than diffuse and were found in some bronchi but were absent in others. Small submucosal masses of granulation tissue or focal areas of scarring were sometimes found (Fig. 2).

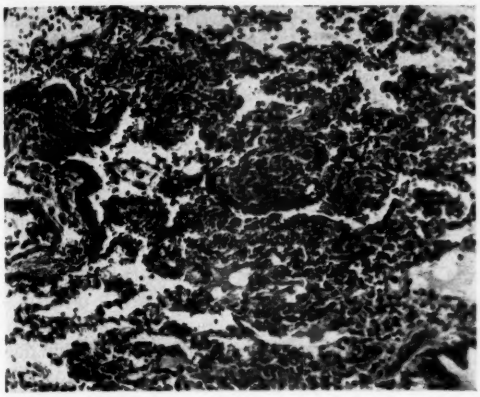

Fig. 12. Photomicrograph of respiratory bronchiole of posterior basic segment in Case 1. Note infiltrate of the wall with extension into the contiguous alveolar walls. This lesion is a typical example of those found at this site in all bronchographically normal and diseased segments. Segment normal bronchographically. ×135.

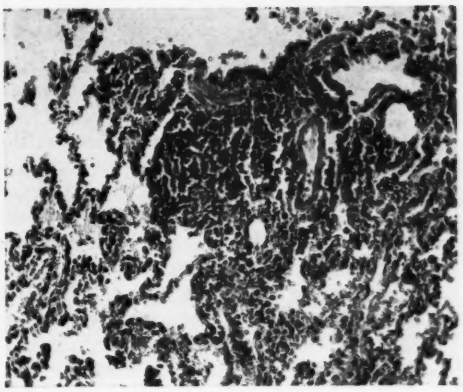

Fig. 13. Photomicrograph of respiratory bronchiole of left anterior middle segment in Case 3. Lymphoid collection present outside muscular coat of bronchiole. Inflammatory cells extending out along interstitial tissue (below and to right and left of bronchiole). Bronchography showed doubtful ectasia. ×138.

Lymphocytic infiltration of the adventitia or adventitial scarring was comparatively common. Nevertheless, the bronchial lesions were minimal in degree.

The bronchioles presented the relatively most marked lesions. The bronchioles were more widely involved by the chronic inflammatory infiltrates and the degree of infiltration appeared slightly more intense. Lymph follicle formation was present and was particularly striking in Case 1. We consider that the amount present was abnormal but have not laid stress on this finding. Submucosal fibrosis of slight to moderate degree was more common than in the bronchi. Thin collars of lymphocytes and neutrophils were present in scattered areas about tiny lymphatics (Fig. 3). The alveolar walls contiguous to involved bronchioles showed variable changes, consisting of focal interstitial pneumonia or fibrosis with epithelization of the lumens. Occasionally one or several alveolar lumens contained a mixed exudate of macrophages and neutrophils. Alveolar expansion as a whole was poor and scattered foci of alveolar wall fibrosis were evident. Intra-alveolar fibrous polyps were occasionally found and in Case 5 they were relatively numerous.

It is useless to speculate on the origin and outcome of these lesions from the histopathologic point of view. It is merely possible to state that definite, if minimal, inflammatory lesions were present.

DISCUSSION

From the clinical point of view, the roentgenologic diagnosis of bronchiectasis is the most reliable guide to the extent of the lesions. For all practical purposes, especially segmental surgery, it is the bronchographic appearance, coupled with examination by the surgeon at the time of operation, which determines the extent of the operative procedure. However, as Pilcher says, the exact value of palpation of the lung at operation has yet to be proved.

Bronchographic diagnosis of bronchiectasis was made in the segments as shown in Table II. The gross and microscopic findings are represented in parallel columns. It is evident that there are segments showing histopathologic inflammatory lesions in which no change was demonstrated by bronchography or by gross examination. The microscopic changes were similar in type to those seen in the segments which showed roentgenographic change but less in degree. The dorsal segments showed histopathologic involvement in every case, minimal in Cases 1, 6, and 7 (Figs. 2, 4, 5, 6, 7, 8, and 9). In only 2 cases, Nos. 4 and

7, was definite involvement demonstrated by bronchography. Case 7 was the converse of the others in that the lesions were minimal while the bronchographic examination showed moderate involvement. In 1 case, No. 2, the bronchus to the dorsal segment was not filled and here the microscopic changes were fairly marked with several minute healing abscesses. The difference between the lesions of the dorsal segments and those of the basic segments appeared to be quantitative only.

That extreme care must be exercised in the interpretation of the roentgenographic appearance in the selection of the segments for resection, is illustrated by the fact that even the more advanced lesions, on occasion, are not accompanied by changes in the roentgenographic appearance. In Case 1, only the bronchi to the anterior basic segment were abnormal, roentgenologically, whereas microscopic examination revealed lesions, as well marked as those of the anterior basic, in the bronchi to the other two basic segments (Figs. 10, 11, and 12). Similarly, in Case 3, only the basic segment bronchi showed dilatation roentgenographically while the anterior middle and lateral middle segments of the lingula were definitely abnormal (Figs. 3 and 13). It may be noted at this point that all the lingular segments were involved to an equal degree. In Case 6 the middle lobe bronchi were only slightly dilated bronchographically, while microscopically the lesions were severe.

It would appear from the foregoing that when disease is present to such a degree as to be visible roentgenographically, the adjacent segments are usually involved by inflammation, though to a lesser degree. It is possible nonetheless that these are early lesions, capable of progressing to either full blown bronchiectasis with permanent dilatation or to temporary dilatation of the reversible type (4, 6), and by the same token it seems equally reasonable to suppose that those inflammatory lesions may regress without the development of bronchial ectasia if the major focus of infection is removed. The relationship between duration of symptoms and the degree of this minimal involvement of segments unaffected grossly could not be determined in this group of cases.

From a purely histopathological viewpoint it is impossible to state whether the lesions were progressive or not. In the segments with very slight involvement, the possibility seemed remote but in the slightly involved segments one could speculate on the possibility of progression. If these lesions were secondary to extension from the involved segments, they might have cleared completely, following segmental resection. On the other hand, it is possible that they represent a persistent low grade inflammatory process following a pneumonitis.

In basic segments, however, where bronchography has not demonstrated dilatation, we have observed lesions as marked as those in segments in which involvement had been shown by roentgenographic examination. Therefore, we believe that extreme caution is necessary in evaluating the extent of the lesions. Correlation with bronchographic changes in these few cases has not been entirely consistent. This perhaps is comprehensible if one accepts the theory that ectasia is a secondary phenomenon depending on the degree of atelectasis and parenchymatous involvement.

SUMMARY

1. The various lobes from relatively early cases of bronchiectasis in children, for which lobectomy (and in 1 case pneumonectomy) had been performed, were dissected segmentally. The distribution of the lesions, as seen roentgenographically, is compared with the gross and microscopic findings.

2. Destructive lesions of bronchi, such as epithelial ulceration and destruction of muscle and elastica, were not a predominant feature.

3. Detailed microscopic examination showed definite if minimal inflammatory lesions of the segments which by bronchographic and gross examination appeared unaffected. These lesions are essentially similar to those found in the affected segments but it is impossible to draw any conclusions as to whether they are progressive or not.

4. The pathologic findings in this small series of cases have not been entirely consistent with the bronchographic appearance. This is

understandable if ectasia is considered as a secondary phenomenon and if visible and definite involvement is not immediately present.

5. Such findings point to the necessity of further detailed study of the various lung segments in bronchiectasis from the clinical, roentgenological, surgical, and pathological aspects.

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VAGOVAGAL REFLEXES

Electrocardiographic Changes During Vagotomy

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CASES of sudden death due to cardiac or respiratory arrest coincident with manipulation of a vagus nerve or its branches during surgery in the neck or thorax have been reported (3). While direct stimulation of cardiac vagal fibers may have occurred, it is the opinion of some (22) that the majority of vagal stimuli, even those arising above the cardiac branches, result in an impulse which takes an afferent path to the medulla. An efferent impulse, completing a reflex, may then return over vagal fibers causing cardiac inhibition. This may be considered an example of a true vagovagal reflex in contrast to some partially nonvagal reflex arcs in which the impulse traverses other than vagus pathways for a portion of the arc.

Operations in which the procedure traumatizes the vagi between the pulmonary plexus and the stomach have increased with the revival of vagotomy for the surgical therapy of duodenal ulcer. To date only 1 apparently authentic case of a vagovagal reflex resulting in cardiac arrest and death during vagotomy has been reported (21). A previous incident in which vagovagal reflexes may have initiated an unfavorable postoperative course which shortly terminated in death has been recorded by Moore and associates.

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Development of the various types of anesthesia in use today has necessitated an evaluation of the effects of preanesthetic and anesthetic medications on cardiac function. These alterations have frequently been conveniently recorded by means of the electrocardiogram. The difficulty of dissociating the effects of surgical manipulation from those specifically resulting from the anesthetic itself have been commented on in these reports, and the predominant role of the vagus nerves in the transmission of the afferent or efferent impulse, or both, has been emphasized.

Electrocardiographic alterations in specific relation to the operation of vagotomy for duodenal ulcer are of interest in further investigation of this problem. These changes would be expected to be subclinical in nature, but might indicate, to some extent, the possibility of more serious sequelae to a vagovagal reflex.

ELECTROCARDIOGRAPHIC OBSERVATIONS DURING VAGOTOMY

Bilateral vagotomy between the pulmonary plexus and the stomach, by a left transthoracic approach, was done on 10 dogs. Another procedure to be described later, which also involved the vagus nerves, was performed on 3 additional animals. No premedication was given and endotracheal ether anesthesia was employed. Anesthesia was maintained at an even depth throughout operation. Standard

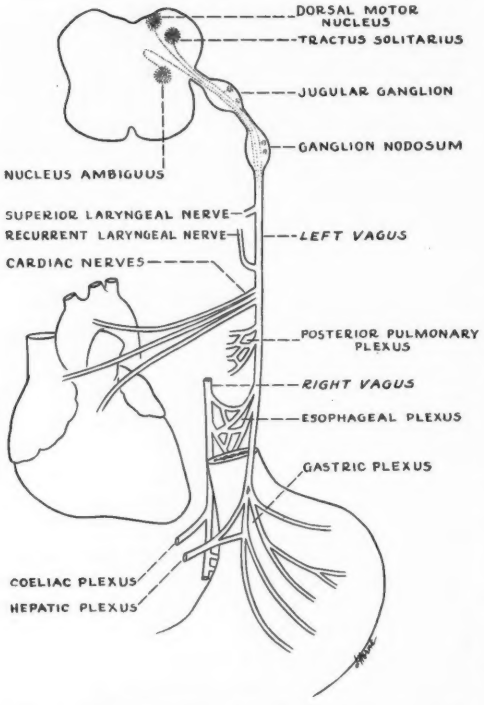

Fig. 1. Diagrammatic sketch of principal vagus pathways.

lead II was utilized in all cases, with the dogs in the right lateral position. Tracings were taken almost constantly, and always during manipulations involving viscera or vagus nerve trunks.

Electrocardiograms were also taken in the cases of 10 humans before, during, and after bilateral vagotomy for duodenal or marginal ulcer. In 4 of these the electrocardiographic tracings during portions of the operative procedure were not entirely satisfactory, and the possibility of transient changes of undetermined type was present. In 6 cases records were complete in every respect. In 5 of these transabdominal operations were performed and in 1 transthoracic was carried out. The usual preanesthetic medications were given, since they do not entirely abolish subclinical changes in cardiac function which occur during surgery and anesthesia.

TABLE I.—ELECTROCARDIOGRAPHIC CHANGES OBSERVED IN 13 DOGS AND 6 HUMANS DURING OPERATIONS INVOLVING SECTION (10 ANIMALS AND 6 HUMANS) OR ISOLATION (3 ANIMALS) OF THE GASTRIC VAGI

Types of electrocardiographic changes observed	No. animals		No. humans	
	Total No. each change noted	No. related to vagal stimulus	Total No. each change noted	No. related to vagal stimulus
Decrease in heart rate	12	3		
Decrease in amplitude, notching, or inversion of *P* wave	12	2	2	
Increase or decrease in amplitude of *R* wave	4			
Prolongation of *P-R* interval	9	1	4	2
Dissociation phenomena	2	1	1	
Nodal rhythm	2		1	
Sino-auricular pause	3	1		
Sinus arrhythmia	6	3	1	
Premature beats	2		1	
Flattening or inversion of *T* waves	3			

All electrocardiographic records taken in the period after induction of anesthesia and before beginning the operative procedure were normal. On 11 occasions during the operative procedures on 5 animals, decreases in rate, changes in amplitude or inversion of the *P* wave, variations of the *P-R* interval, dissociation phenomena, or sinus arrhythmia and sino-auricular block, were thought to have been specifically related to manipulations of the vagus. Similar and other changes also occurred without relation to visceral or vagal stimulation. All changes observed during operation without exception reverted to normal simultaneously with, or shortly after, closing the chest. Factors such as artificial respiration, direct stimulation of the heart, endotracheal intubation, and irritant effects of anesthetic vapors cannot be entirely eliminated.

Changes apparently related to handling of a vagus nerve occurred in 2 humans. These changes consisted of a lengthening of the *P-R* interval. Other electrocardiographic abnormalities seen in the humans were not related to a specific mechanical stimulus. In only 1 clinical case did any electrocardiographic change

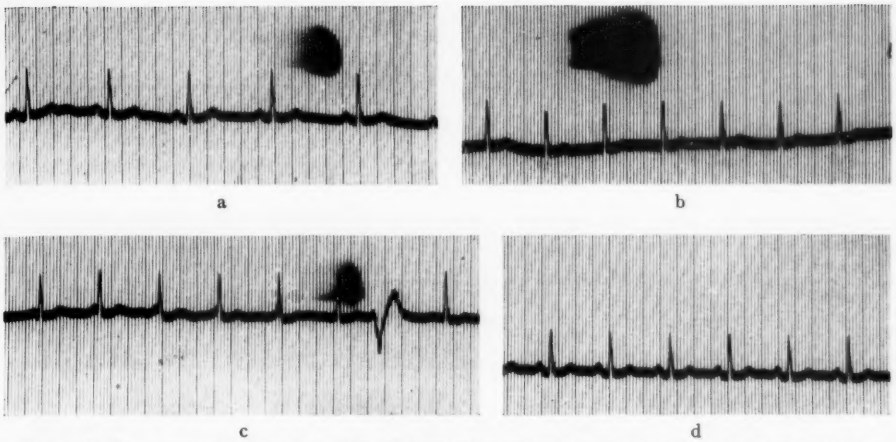

Fig. 2. S. W., 50 year old white male. Transabdominal vagotomy for peptic ulcer. Standard lead II. a, Patient under ether anesthesia prior to surgery, sinus rhythm. b, During manipulations of esophagus preparatory to isolation of vagi. Middle nodal rhythm. The fifth complex is suggestive of a low nodal beat with inverted *P* wave superimposed on *T* wave. c, Recorded shortly after b. Interference dissociation with 1 ventricular premature beat. d, Immediately postoperative; sinus rhythm.

show in the postoperative tracings. This patient had a normal preoperative electrocardiogram, but demonstrated an inverted *P* wave during most of the time that a vagotomy was being done. This reverted to normal before the patient left the operating table, and remained so the next day. Electrocardiograms taken on the second, third, fourth, and fifth postoperative days showed a reappearance of the inverted *P* wave. Explanation of this single instance of change in the postoperative tracings would be purely speculative.

If electrocardiographic abnormalities were noted they usually occurred early in the operation about the time that the first exploratory movements for the nerves were being made. Opening of the chest in the animals was never immediately followed by change in the electrocardiogram. When major changes in cardiac rhythm appeared they exhibited a definite tendency to persist throughout the remainder of the operation, and additional manipulation of viscera or nerve trunks failed to induce further change. There was no apparent relation to duration or depth of anesthesia.

In 3 animals bipolar electrodes attached to insulated wires leading from the chest were secured to one of the vagal trunks along the lower esophagus. Electrocardiographic tracings were taken during surgery while the animals were under endotracheal ether anesthesia and repeated 24 hours later without anesthesia. Two animals showed no significant electrocardiographic change either during the operative procedure or during mechanical and faradic stimulation of the vagus 24 hours later. The third animal showed nodal rhythm and dissociation phenomena when traction was applied to the left vagus and this abnormality persisted until shortly after the chest was closed. Twenty-four hours later, without anesthesia, mechanical and faradic stimulation of the vagus caused a slight decrease in the amplitude of the *P* wave, occasional premature beats, sinus arrhythmia, and a brief sinoauricular pause. Conclusive evidence that cardiac effects will usually follow stimulation of the gastric vagi in the absence of anesthesia was not obtained from these experiments.

DISCUSSION

The numerous electrocardiographic studies which have been recorded during surgery and anesthesia are in some disagreement concerning the relative importance of visceral stimulation and that of the anesthetic in initiating these alterations. Some have felt that the anesthetic was the predominant fac-

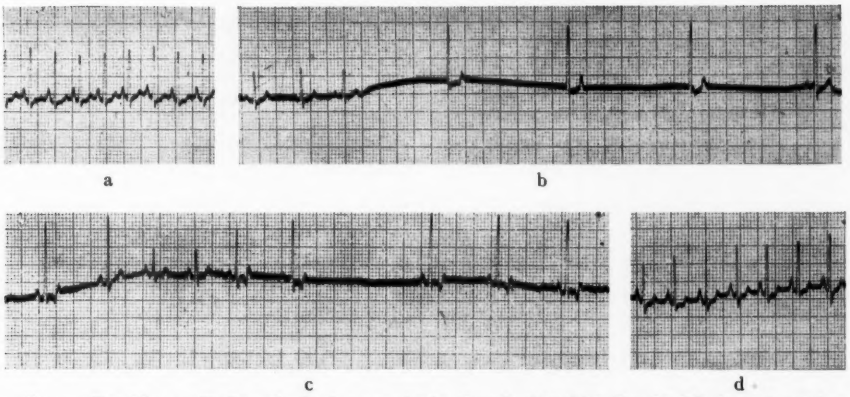

Fig. 3. Dog No. 5. Endotracheal ether anesthesia. Standard lead II. Dog in right lateral position. a, Surgical anesthesia prior to surgery; sinus rhythm, rate approximately 215. b, Changes occurring during manipulation of esophagus preparatory to isolation of the nerves (left thoracic incision, positive pressure anesthesia). *P* wave changes in first three complexes suggest shift in sino-auricular pacemaker followed by a middle nodal escape and midnodal rhythm for 2 beats. The sixth complex is a lower nodal beat. The impulse for the last complex arose in the sino-auricular node. Rate decreased from approximately 104 to 42. These changes persisted throughout surgery and were not influenced by actual clamping or traction of vagi. c, Vagotomy completed, chest still open. Variation in shape of *P* waves indicates shifting pacemaker in sino-auricular node. There is a period of sino-auricular block after the sixth complex followed by return to sinus rhythm. Variations in height of *R* waves may be attributed to respiratory effect. d, Chest closed; surgical anesthesia maintained; sinus rhythm; rate approximately 166.

tor (12), while others have indicated the frequent relation of the electrocardiographic changes to operative manipulation (10). The occurrence of cardiac abnormalities with anesthesia only, during anesthesia before beginning an operative procedure, and after conclusion of an operation, indicates that manipulation is not a prerequisite. However, in many instances, there undoubtedly is a relationship between the manipulation and the cardiac changes. The results in this series emphasize the etiological importance of mechanical stimuli occurring during surgery. It is also probable that the anesthetic sensitizes certain tissues, and the result is a response to stimuli which would otherwise be ineffective (14).

The fact that in a few instances stimulation of the gastric vagi seemed directly to initiate alterations in cardiac rhythm suggests that the vagi serve as the afferent path for some viscerocardiac reflexes. Such reflexes are more frequently associated with surgery in the upper abdomen, where vagal endings are more numerous than in the lower abdomen. It has been shown experimentally that cardiac inhibition produced by stimulation of exposed viscera can be prevented by section of the gastric vagi (5), but confirmation is lacking in man. That afferent pathways other than vagal may be utilized is demonstrated by the association of viscerocardiac reflexes with stimulation of areas in which there are no vagal endings (10, 12).

The similarity of the electrocardiographic changes which occurred during this series of vagotomies to those resulting from vagal stimulation proximal to the heart is striking. Proximal vagal stimulation has been known to cause sinus arrhythmia; bradycardia, cardiac arrest; changes in the *P* wave, such as flattening, notching, and inversion; prolongation of the *P-R* interval; dissociation phenomena; nodal rhythm; complete auriculoventricular block; premature contractions; variations in the amplitude of the *R* wave, and flattening to the *T* wave. All operative procedures in this series interrupted the vagi distal to the pulmonary plexus, and no specific vagal stimulation other than that usually incident to a vagotomy was done. Nevertheless, all the changes, without exception, which were cited previously as occurring after stimulation of

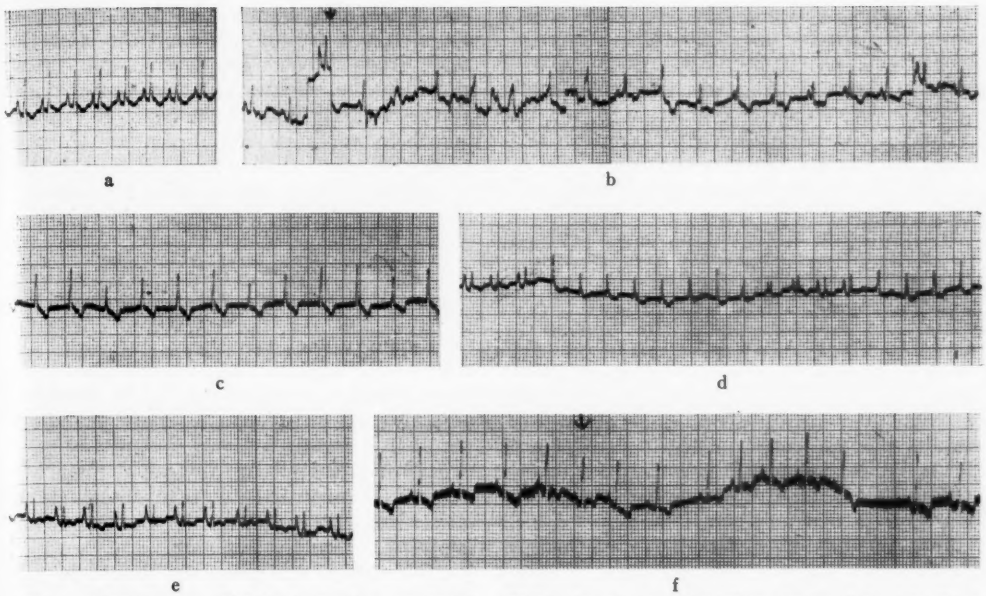

Fig. 4. Dog No. 10. Endotracheal ether anesthesia. Dog in right lateral position. Standard lead II. a, Dog anesthetized prior to surgery; sinus rhythm, rate approximately 214. b, Left thoracic incision; positive pressure anesthesia. The first two complexes represent sinus beats. At point indicated by arrow left vagus nerve traction was applied. Immediately thereafter numerous artifacts are recorded but interference dissociation is noted to be present. c, Recorded several minutes after b. Middle nodal rhythm with phasic respiratory variations in *QRS* voltage. d, Wiring of vagi completed. Sinus rhythm (3 beats). Sino-auricular block followed by nodal escape with middle nodal rhythm for 7 beats and subsequent interference dissociation. e, Chest closed but surgical anesthesia maintained; sinus rhythm. f, Recorded 2 days later; dog unanesthetized. Traction put on vagi by pulling previously placed wires at point indicated by arrow. Marked sinus arrhythmia with 1 short period of sino-auricular block (just preceding last two complexes).

the proximal portion of the vagus, were seen at least once in this series of electrocardiographic tracings.

The clinical importance of these electrocardiographic changes should not be overestimated. Alterations in cardiac rhythm have been seen following gaseous eructations, nausea and vomiting, passage of gastric tubes, bronchoscopes, and endotracheal tubes, and deep respirations.

Cardiac abnormalities resulting from anesthesia are not only due to the direct effects of the anesthetic on the heart. In addition to increased sensitivity and irritability of cardiac tissue, changes in the physiologic efficiency of the conduction mechanism and alterations in vagal tone are conditions resulting from anesthesia which render the vagi and the heart more receptive to a given stimulus. Receptivity also varies among individuals, and in each individual at different times. Since the type of anesthesia and preanesthetic medication chosen can usually be to some degree elective, it is of advantage to examine the experimental and clinical experience indicating that some anesthetic and preanesthetic medications have selective actions on the vagus mechanism and cardiac tissue, while others are less likely to be productive of cardiac abnormalities.

Of the agents most frequently used in inhalation anesthesia, cyclopropane is well known as the chief offender in the production of cardiac irregularities. While vagotomy did not abolish all such irregularities under cyclopropane anesthesia, an absence of increase in the *P-R* interval suggested that there was no disturbance in conduction (17). Few signifi-

cant electrocardiographic changes have been observed with the use of ethylene (10) or nitrous oxide, except for those associated with anoxia (20). Ether, a sympathomimetic agent, depresses vagal conduction (9, 19), but sensitizes the auriculo-ventricular node relatively more than the sino-auricular node, resulting in escape phenomena and shifting of the pacemaker (15).

Barbiturates decreased response to vagal stimulation but sodium pentothal (a thiobarbiturate) failed to demonstrate such a protective action (7). Though morphine has been said to increase vagal tone (17, 18), in the usual clinical dosage it may not be apparent (1). Any bradycardia resulting from the administration of morphine probably is a result of blocked cortical impulses which normally inhibit the vagal medullary center (2).

The effects of atropine in depressing the response to ordinary vagal stimuli are well known, but Lennox and Levine found that the usual doses only decreased electrocardiographic changes by one-half. Small doses are ineffective in achieving complete vagal paralysis and if this drug is being used to afford protection from the effects of vagal stimulation, a combined total of preanesthetic and intravenous doses should be 1.5 to 2.0 milligrams. Actual stimulation of the vagus center may be the initial result of small doses of atropine.

Experimentally, curare rendered the heart unresponsive to vagal stimulation (4), though ineffective in the presence of asphyxia (13).

An immense number of gastric resections and numerous experimental procedures requiring section of the gastric vagi have been done. The rarity of reports of clinically apparent cardiac derangements immediately resulting from these procedures makes the danger of a vagovagal reflex seem slight indeed. It is possible that vagovagal reflexes of a serious nature occur more often with surgery involving the more proximal portions of the vagi.

If precautions to avoid an occasional mishap during vagotomy are to be taken, certain recommendations can be made. These are selected after a consideration of some known specific actions, some of which are described in the preceding paragraphs, of the agents in common use during surgery. The effects of these drugs on vagal conduction would seem relatively more important than their actions on the intrinsic tissue of the heart, in evaluating their worth in the prevention of vagovagal reflexes.

1. Barbiturates and atropine are indicated for preanesthetic medication. Morphine is probably best omitted.

2. Ether is the anesthetic of choice.

3. If curare is employed during the operative procedure it can be counted on to afford additional protection.

4. Good oxygenation is imperative.

5. Atropine, in adequate dosage, should be administered intravenously before search for the vagi is begun.

6. Procainization of the vagal trunks is necessarily preceded by mechanical stimulation incident to isolation of the nerves and is of little prophylactic value.

7. A section of the nerves should be carried out with a minimum of traction or other trauma.

8. Ligation of the central ends of the nerves should not be done routinely. It has been noted that ligation (6) and pinching the nerve with forceps (8) effectively initiated afferent stimuli.

CONCLUSIONS AND SUMMARY

1. Numerous reports indicate that subclinical changes in cardiac function, as determined by electrocardiography, frequently occur during surgery and anesthesia.

2. Observations on a small series of clinical and experimental cases during section of the gastric vagi demonstrated that electrocardiographic changes similar to those previously observed during other surgical procedures are not uncommon.

3. The comparative frequency of these subclinical derangements in cardiac rhythm is not a true indication of the relative incidence of vagovagal reflexes which would result in serious cardiac disturbances. The danger of such an occurrence during vagotomy for peptic ulcer is remote.

4. If the maximum precautions available are desired, recommendations concerning pre

medication, anesthesia, and avoidable mechanical stimuli during operation have been made.

5. The preceding conclusions and recommendations may only be applicable to cases in which the vagal stimulus arises below the pulmonary plexus.

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EFFECT OF PANCREATIC JUICE ON THE GALL BLADDER

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SINCE the main pancreatic duct empties into the duodenum in conjunction with the common bile duct, an ampulla of variable length is formed. Conceivably, conditions are present for an obstruction of the ampulla to create a continuous pathway between the biliary system and the pancreas (Fig. 1). The causes of obstruction have been listed as resulting from stones (24), spasm of the sphincter of Oddi (3), and acute edema of duodenal mucosa in the region of the ampulla (5). A continuous pathway can be demonstrated clinically by cholangiography. Dye injected into a T tube will sometimes fill the main pancreatic duct when the ampulla is obstructed.

DIRECTION OF FLOW

If a common channel of the biliary tract and pancreas is formed, the question arises: Will pancreatic juice reach the gall bladder? The pressure in the two systems has been measured in the experimental animal by many investigators (18, 19, 21, 27, 17, 14, 28), and the secretory pressure of the liver was found to equal that in the pancreas. These changed with the varied stages of digestion. Wolfer (36) introduced India ink into the terminal end of the common bile duct and found that at times it reached the gall bladder.

Clinically there is evidence to show that pancreatic juice can reach the gall bladder. Seifert observed diastase in bile in a clinical case. Walters and Marshall reported 4 cases in which pancreatic juice drained from a T tube, with resulting skin digestion. Popper (25) reported an analysis of bile for pancreatic ferments in 219 operative cases. Seventeen per cent showed increased diastase values, but 7 per cent were in cases of pancreatitis. In 36 of the cases bile was obtained by puncture of the gall bladder in the course of operations for conditions unrelated to the biliary tract or pancreas. In 3 of these, pancreatic ferments were obtained.

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PATHOLOGY

If it is assumed, then, that pancreatic juice does reach the gall bladder, will pathologic changes result? It is known that active pancreatic juice can digest living tissue, as is demonstrated in the skin surrounding a high intestinal fistula. One would expect the gall bladder to be attacked by these enzymes, since this viscus is a very delicate structure. Schönbauer reported a case of gangrenous cholecystitis with biliary exudate in the peritoneal cavity. Trypsin was present in the bile. Westphal introduced duodenal secretions into the gall bladder in dogs and produced changes which in some approached necrosis. Wolfer (37) introduced pancreatic juice into gall bladder in dogs in a variety of ways and produced a pathologic condition in all instances, ranging from inflammatory cells, focal areas of necrosis with some evidence of regeneration to completely gangrenous structures. Andrews and his associates (2) tested the effect of pancreatic juice on the absorptive mechanism of the gall bladder. They used 19 dogs and injected pancreatic juice, either into the gall bladder directly with a needle or via a ureteral catheter up the common bile duct. All the gall bladders showed mild pathologic changes. Some of the juice was Berkefeld filtered, and less changes were produced in these instances than in those injected with unfiltered juice. Brackertz studied the effect of pancreatic juice on rabbits' gall bladders. He concluded that active sterile pancreatic extract alone had no effect on biliary passages within 12 hours. When colon bacilli were introduced with the pancreatic extract and when the common duct was ligated, digestive necrosis of the gall-bladder wall developed in every case within 12 hours. This necrosis was followed invariably by biliary peritonitis without macroscopic evidence of perforation. The extent of necrosis depended upon the activity of the pancreatic extract. The mucous membrane was attacked first. When pancreatic extract and colon bacilli were injected into the

biliary passages of rabbits without stasis, no change was noted in the gall bladder.

Stulz and Bauer injected active pancreatic juice directly into the gall bladder in dogs and produced pathologic changes. They concluded that chronic changes occur when large amounts of pancreatic juice are injected into the gall bladder, but not necrosis. It must be assumed that the injection of large amounts of ferment means increased pressure within the gall bladder. This may, in itself, cause traumatic changes. Colp and his associates (13) reported 3 cases of free bile in the peritoneal cavity, with fat necrosis in 1. The gall-bladder bile was definitely alkaline in all 3. Diastase was present in large amounts in the bile aspirated from the 3 cases. They concluded that the pancreatic enzymes get to the gall bladder by reflux. The gall bladders showed acute ulcerative changes in the mucosa, and to a less extent throughout the wall. No actual perforation could be identified. They concluded that, if pancreatic juice is found in the gall bladder in such amounts as to change the *p*H to alkaline, digestion of gall bladder occurs. Bisgard and Baker reported 2 cases of acute nonperforating gangrenous cholecystitis with regional bile peritonitis. Cultures from the abdominal fluid, bile, and gall-bladder contents were sterile, but the gall-bladder bile in both cases contained amylase and trypsin. The peritoneal fluid was not examined for enzymes. They experimented on goats, and temporarily or permanently obstructed the common bile duct at various levels, either distal to the cystic duct or distal to the cystic and pancreatic ducts. The duct arrangement in goats is particularly well adapted to the experiment. It was concluded that neither stasis of bile nor reflux of pancreatic juice as a single factor was productive of cholecystitis, but when they were combined they produced permanent pathologic changes in the gall bladder. Their combination produced a complete or partial necrosis of the gall-bladder wall which was chemical and not infectious. In several goats there was a nonperforating biliary peritonitis. They concluded that filtered bile does not activate pancreatic enzymes.

Aronson anastomosed the pancreatic duct to the gall bladder in 4 dogs. All remained well for 2 years. They were then sacrificed, and it was found that in 3 the anastomosis had scarred over, and in 1 the anastomosis was open. There were extensive adhesions between the gall bladder, pancreas, and duodenum. The gall bladder was dilated and contained 25 cubic centimeters of a grayish-brown cloudy fluid and 3 stones. Cultures of bile revealed Staphylococcus aureus and Clostridium welchii. Only slight changes were found in the gall-bladder wall, and the author concluded that this was because the pancreatic juice was very considerably diluted with bile. Gatch and his associates injected activated pancreatic juice into the ampulla of Vater in 3 dogs. In 1 the injection was under considerable force, and the dog died in 15 minutes. Beginning necrosis around the bile ducts in the liver was found. In the remaining 2 animals, the injection was made with moderate pressure, and only minor changes in the bile ducts resulted. The writers concluded that the pancreatic juice acted for only a short time and that great damage would result if stasis of bile had prolonged the action of the pancreatic juice. The mechanical effect of the increased intraductal pressure is a factor that must be reckoned with in this experiment.

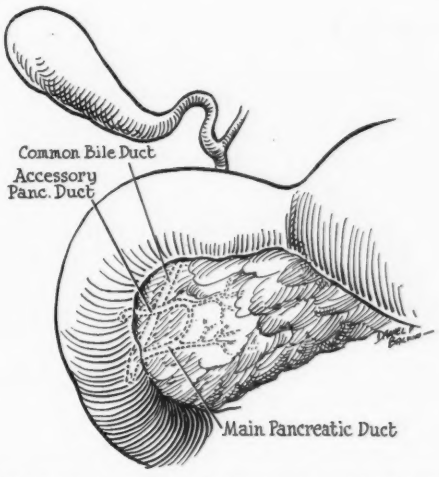

Fig. 1. The ampulla in the human—formed by the junction of the common bile duct and the main pancreatic duct.

Nonperforating biliary peritonitis, mentioned previously, is undoubtedly a definite

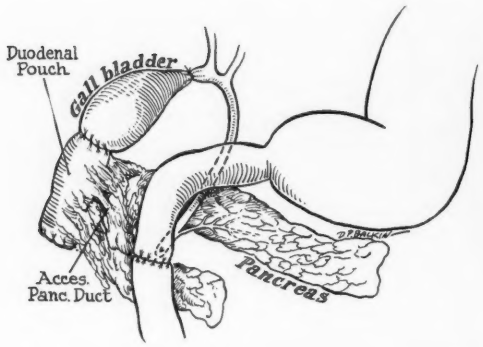

Fig. 2. Procedure used in the experiment to introduce pancreatic juice into the gall bladder in dogs.

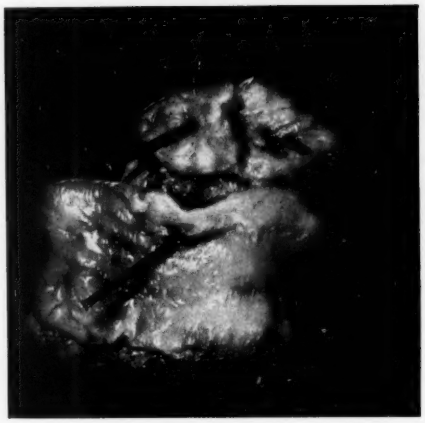

Fig. 3. The duodenum, gall bladder, and duodenal pouch have been cut open. The shorter probe shows the opening of the lesser pancreatic duct in the duodenal pouch. The triangular tissue on the right, anastomosed to the pouch, is the gall bladder, with the ligated cystic duct shown at its apex. The longer probe lies in the common bile duct and demonstrates the papilla of Vater. The puckered line to the left of the ampulla is the point of anastomosis to re-establish the continuity of the duodenum. Notice its proximity to the papilla. Pancreas is seen in the background.

pathologic entity. The first case recorded in the literature was reported in 1910 by Clairmont and Haberer, who offered no explanation for the condition. In 1918, Blad produced biliary peritonitis with microscopic necrosis of the gall bladder by introducing pancreatic juice into the gall bladder. He concluded that bile is capable of traversing an animal membrane exposed to pancreatic juice. He opined that bacteria plus pancreatic juice digested the colloids of bile and liberated pigment, which passed through the gall-bladder wall.

In 1927, Bundschuh reported a case of a stone at the ampulla with nonperforating biliary peritonitis in which pancreatic enzymes were isolated from the peritoneal cavity. Ruppaner reported a similar case the following year. In 1930, Popper (26) reported a case of biliary exudate in the peritoneal cavity with fat necrosis of the omentum. The gall bladder was enlarged and thickened, the common bile duct was dilated, the pancreas showed little change and there were no stones in the ducts. Trypsin was isolated from the gall bladder and questionably in the peritoneal exudate. The common bile duct was drained, and pancreatic ferments temporarily flowed from the fistula. Bernhard and Dziembowski, in 1931, each reported a case. The latter explained the findings on the basis of abnormal conditions leading to diffusion of contents through the wall of the gall bladder. When the common duct is obstructed, he believes that large amounts pass through the wall of the gall bladder, preventing jaundice. Bernhard reviewed the literature and found reports of 70 cases of nonperforating biliary peritonitis made since Clairmont and Haberer's case report in 1910. In 1934, Melchoir reported 3 cases, and in 1938 Colp and Doubilet (12) reported an additional one.

In 1932, Andrews and associates (1) showed that pancreatic juice in dogs caused prompt changes in permeability of the gall bladder to bile salts, which are rapidly absorbed. There was a profound fall in the bile salt cholesterol ratio to a very low level, while the cholesterol content of the bile remained about the same. About one-third of the bile salts were absorbed, and in many, especially with unfiltered juice, all the bile salts were absorbed. In 1944, Mirizzi concluded that it was not the pancreatic secretion itself that caused the change, but that the reaction of bile from acid to alkaline makes a good medium for activating trypsin to the point to where it digests tissue. Watson states: "Regurgitation of pancreatic juice into the biliary tract may at times play a role in the etiology of cholecystitis."

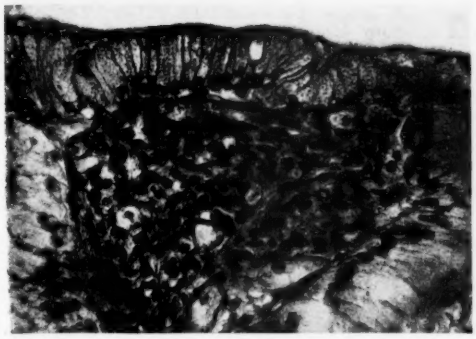

Fig. 4. Dog No. 54. Gall bladder 190 times. Showing scattered polymorphs in stroma of mucosa.

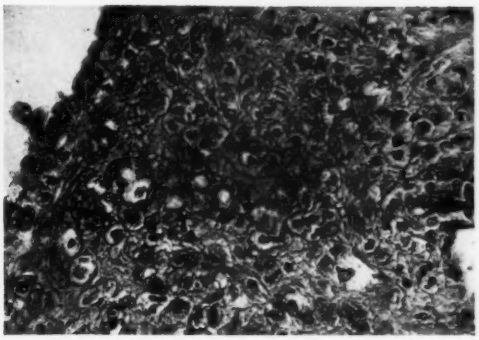

Fig. 5. Dog No. 60. Gall bladder 190 times. Many acute inflammatory cells are seen.

EXPERIMENT

An experimental procedure was designed to show the effect of pancreatic enzymes on the gall bladder under as nearly physiologic conditions as possible. Dr. Andrew C. Ivy suggested the procedure, which was followed throughout the experiment.

Average sized mongrel dogs were used. The abdomen was aseptically entered, the duodenum was brought out on the abdomen and the lesser pancreatic duct identified without jeopardizing the blood supply. The location of the papilla of Vater was estimated. Midway between the pancreatic duct and the papilla the duodenum was transected, the gastroduodenal vessels being avoided. About 3 centimeters distal to this point of section, the duodenum was again sectioned, and a short segment of bowel containing the pancreatic duct with the pancreas and blood supply intact was isolated (Fig. 2). One end of this duodenal pouch was closed and the other was anastomosed to the fundus of the gall bladder. The continuity of the duodenum was then re-established. By this procedure the pancreatic juice entered the duodenal pouch in the normal manner, flowed over the gall-bladder mucosa and drained from the cystic duct into the duodenum. The duct of Wirsung in the dog plays a very minor role.

Dogs recovered and remained well. About 3 weeks later the cystic duct was cannulated and secretin was injected intravenously. The contents of the gall bladder were collected and assayed for pancreatic juice. Sections of the liver, gall bladder, and pancreas were taken and the patency of the pancreatic duct was demonstrated (Fig. 3). *No pathologic condition was found in the gall bladder in the 10 dogs in this first series.*

Another group of 10 dogs were subjected to the same preliminary procedures, but 3 weeks later the cystic duct was ligated. The animals became moribund within 100 hours. The contents of the gall bladder were assayed for pancreatic enzymes, the same sections were taken and the patency of the pancreatic duct was again demonstrated.

Results. Six dogs showed an acute reaction of the gall bladder (Figs. 4 and 5), one having complete necrosis (Fig. 6). Two dogs

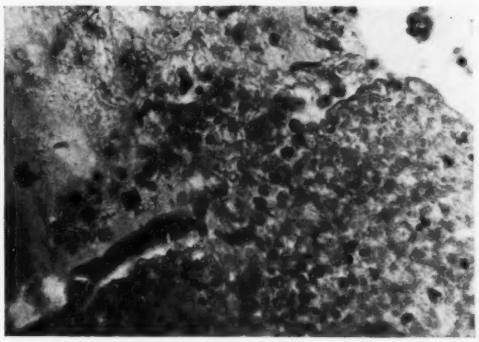

Fig. 6. Dog No. 57. Gall bladder 190 times. Showing ulceration of the mucosa with acute inflammatory and ghost cells.

showed acute pancreatitis. In 2 dogs there was a leak at the anastomosis. Five dogs showed fat necrosis of omentum in region of gall bladder. Peritonitis was found in all 10 dogs. Seven animals showed a pathologic condition in the liver.

CONCLUSION

On the basis of this experimental study, it is concluded that pancreatic juice as a single factor has no effect on the gall bladder. However, pancreatic juice plus stasis causes a pathologic condition in some instances.

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MORBID FACTORS IN EXPERIMENTAL APPENDICITIS

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TO gain a more fundamental concept of the basic pathogenic pattern of appendicitis and its chief complicating factor, peritonitis, we have produced this disease experimentally in the dog with the purpose of analyzing those factors which play a role in the production of the morbid process. We have endeavored to evaluate the relative importance of various generalized and local elements associated with appendicitis. The ultimate aim has been to obtain sound experimental data which will be of value to the clinical surgeon in his understanding and treatment of appendicitis and peritonitis. The role of the sulfonamides, penicillin, and other antibiotics has not been considered. Our effort has been directed toward the underlying pathological pattern of the disease process in order to formulate certain principles upon which a rational use of these drugs may be based.

Although considerable experimental work on appendicitis has been undertaken, only a few examples need be cited as representative of two main theories which have evolved regarding the cause of death and pathogenesis of the disease. The first of these general concepts proposes that the local site of infection, the gangrenous appendix, is the focus from which the whole morbid process arises and any systemic alterations are the result, or reflection, of factors which have their origin at this point. The bacteria associated with this gangrenous process have been held responsible for the death of the animal because of a fulminating infection or toxemia. Those workers who have endeavored to show that bacterial toxins are of prime importance have produced only indirect evidence, by means of animal immunization and inoculation of the material in question. An equal number of workers have presented data to show that the products of autolytic digestion are of primary importance. Regardless, however, of the factor, or combination of factors, which bring about the death of the animal, this general concept presents the local site of infection as the initiating factor in the disease mechanism.

The second hypothesis which has been presented as an explanation for the morbidity or mortality in appendicitis and peritonitis places the emphasis on generalized systemic alterations in the animal, factors which are either already present prior to the disease, or which are activated early in the process. The dysequilibrium of circulating enzyme systems, or the depression of various hepatic functions, has been held responsible. When a sufficient alteration of the systemic processes has occurred, the animal is said to be in a morbid or moribund state.

Although no clear cut differentiation of these two general hypotheses has ever been presented, almost all the work which has been done on this subject can be placed in one or the other categories.

Our present study has been undertaken in an effort to obtain a clearer concept of which of these hypotheses is the more important and which factor, or factors, of that hypothesis are the most significant.

THE EXPERIMENTAL DISEASE

Any study of an experimental disease necessitates a careful observation of the normal progress of the disease in the animal used in the study. Since it was our objective to study those factors associated with morbidity or death arising from appendicitis, we endeavored to produce this disease as consistently as was possible in the dog.

In 1938, Bower and his co-workers (2) found that 50 per cent of dogs will recover spontaneously, with no treatment whatsoever, after the appendiceal blood supply and the base of the appendix have been ligated. In every case of recovery, a walled-off appendiceal abscess was found when the dog was sacrificed. Further investigation by the same

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TABLE I.—DISTRIBUTION OF DEATH IN SERIES I DOGS—CONTROL

Mortality, 75%; Average duration of life, 68 hours.

Survived—hours	No. of dogs	Survived—hours	No. of dogs
0 to 24	2	72 to 96	3
24 to 48	8	Over 96 hours	2
48 to 72	3	Lived	6

workers showed that by giving 54 cubic centimeters of castor oil immediately after operation, the mortality rate was increased to 91.7 per cent, and in every case the animal died of a spreading peritonitis.

Twenty-four animals served as our control series. The dogs were given morphine followed by intravenous nembutal as an anesthetic agent. The abdomen was shaved clean and then painted with 1 per cent iodine followed by 70 per cent alcohol. Strict asepsis was followed throughout except that rubber gloves were not worn by the surgeon. A lower midline, or right rectus incision was made and the cecum and appendix mobilized (Fig. 1). All vessels of the appendix were clamped and ligated and a heavy cotton ligature was placed about the base of the organ. Care was taken not to rupture the serosa, and no further crushing of the appendix was done (Fig. 2). The abdomen was then closed in three layers with fine black silk. A gastric tube was placed in the stomach and 50 cubic centimeters of castor oil were given the dog immediately before returning him to the cage. No supportive treatment of any kind was given to the animals and they were disturbed only once a day during the morning when blood samples were drawn. Food and fluid were offered freely following surgery.

The mortality rate for this control series (series I dogs) was 75 per cent and the average duration of life of those animals which died was 68 hours (Table I).

By performing careful postmortem examination on all dead animals and by sacrificing others at appropriate times, we were able to follow closely the progress of the pathological process.

Following recovery from the initial shock of the anesthesia and surgery the animals appeared to go into a lethargic state which slowly progressed until the animal eventually succumbed. This lethargy was associated with a gradually increasing tachycardia and, in many cases, a mild hyperpnea.

Pathologically, within 24 hours the appendix had become a loosely hanging, yellowish-grey necrotic sac with little or no walling-off by the surrounding viscera or omentum. The abdominal cavity contained a small amount of bloody fluid but the abdominal viscera still had a normal glistening appearance (Figs. 3, 4). In this series of 18 control deaths, only two animals deviated from this pattern. One died after 25 hours and another after 26 hours. Both animals had ruptured appendices and peritonitis.

From 24 to 48 hours, the dogs entered the critical period of the disease and at that time the natural body defense mechanisms were brought into play. Early in this period the omentum and loops of bowel began to wall-off the necrotic appendix and a thin layer of fibrin was laid down. A moderate amount of bloody gray fluid was present in the peritoneal cavity (Fig. 5).

The fate of the dog depended on a balance of factors operating during this period. If complete walling-off occurred at this stage, the dog began to recover and survival resulted. If rupture of the appendix occurred before any significant walling-off had taken place, the animal died within 12 hours of a fulminating peritonitis. When a partial walling-off occurred, so as to prevent a rapid dissemination of the gangrenous material into the abdominal cavity, the dog continued to live past the 48 hour period and the eventual length of the survival appeared to be the reflection of the severity of those elements which operated during this stage. Eight of the control animals died during the period between 24 and 48 hours.

All of the animals which managed to survive beyond the 48 hours but then succumbed showed the same pathological picture. The peritonitis increased in severity and no further walling-off of the gangrenous area was seen, as compared with the period up to 48 hours. The omentum was slimy and necrotic, the exudate darkly hemolytic and foul smelling, and the bowel was injected and dull in appearance (Fig. 6). Six of the control animals

Fig. 1.

Fig. 2.

Fig. 3.

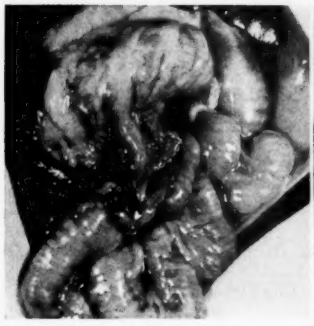


Fig. 4.

Fig. 5.

Fig. 6.

Fig. 1. Normal abdomen of the dog showing cecum, terminal ileum, and appendix.

Fig. 2. The appendix as it is ligated to produce experimental appendicitis in the dog.

Fig. 3. The ligated appendix and peritoneal cavity after 16 hours. This appendix appears as a black gangrenous sac. This type of necrosis is often seen in early stages of the disease.

Fig. 4. The ligated appendix and peritoneal cavity after 26 hours. The loosely hanging, yellowish gray necrotic sac has been walled-off very little by the surrounding viscera and omentum. There is a minimal amount of thin bloody exudate in the peritoneal cavity. The bowel has a normal glistening appearance.

Fig. 5. The ligated appendix and peritoneal cavity after 48 hours. The omentum is injected and has been partly dissected away from the gangrenous appendix. The abdominal cavity contains a considerable amount of reddish brown exudate.

Fig. 6. The necrotic appendix and abdominal cavity 72 hours after the disease was produced. The slimy injected omentum has been partly dissected away from the appendix. The abdominal cavity contains considerable dark, hemolytic, foul smelling exudate.

died during the period from 48 to 96 hours. Only 2 lived beyond this time, 1 of which died after 104 hours and the other after 168 hours.

With this pathological pattern of response to the experimental disease as a background, the specific evaluation of generalized and local factors was undertaken.

GENERALIZED FACTORS IN EXPERIMENTAL APPENDICEAL PERITONITIS

In 1946, Kay and Lockwood (12, 13) made a careful study of various systemic alterations occurring in experimental appendicitis in the dog. They concluded that this disease, "culminates in an acute toxemia characterized by profound disturbances in hemodynamic equilibrium and in impaired function of the liver, lungs and other vital organs." They also suggested that, "the outcome of the disease, regarding death or survival appears to be related more to factors inherent in the condition of the animal prior to the experiment than to any demonstrable bacteriologic or anatomic variation in the local lesions as between dying and surviving animals."

TABLE II.—PLASMA FIBRINOLYSIS IN SERIES I DOGS

Dog	Outcome	Prior to surgery	24 hr.	48 hr.	72 hr.	96 hr.	120 hr.	144 hr.
1	D-25hr.	Negative	Negative					
2	D-96hr.	Negative	Negative	Negative	Negative			
3	D-48hr.	Negative	Negative	Negative				
4	Lived	Negative	Negative	Negative	Negative	Negative	Negative	Positive 48 hrs.
5	Lived	Negative	Negative	Negative	Negative	Negative	Negative	Negative
6	D-168hr.	Negative	Negative	Negative	Negative			
7	D-36hr.	Negative	Negative					
14	D-48hr.	Negative	Negative					
15	Lived	Negative	Negative	Negative	Negative	Negative	Negative	
16	Lived	Negative	Negative	Negative	Negative			
17	Lived	Negative	Negative	Negative	Negative			
18	D-96hr.	Negative	Negative	Negative	Positive 48 hr.			
19	D-90hr.	Negative	Negative	Negative	Positive 48 hr.			
20	D-50hr.	Negative	Positive 48 hr.					
21	D-104hr.	Negative	Positive 48 hr.	Negative	Positive 48 hr.	Negative		
23	D-26hr.	Positive	Positive 48 hr.					
25	D-48hr.	Positive	Negative	Negative				
26	D-72hr.	Negative	Negative	Negative	Negative			
28	D-72hr.	Positive	Positive	Negative				
29	D-48hr.	Positive	Positive					
30	Lived	Negative	Negative	Negative	Negative	Negative		
32	D-48hr.	Negative	Negative					
35	D-72hr.	Negative	Negative	Negative				
47	D-48hr.	Negative	Negative					
24	6 survivals 18 deaths	4	5	0	3	0	0	1

Average length of survival, 68 hours.
D, death

The same authors also studied the balance between fibrinolytic and antifibrinolytic factors in the blood of animals with experimental appendiceal peritonitis and concluded that a much greater frequency of spontaneous lysis of plasma fibrinogen and fibrin occurred in those animals which died than in those which survived.

These investigators also obtained results which would indicate that those animals which survived showed no abnormality in prothrombin time immediately prior to the onset of the crisis, while those which succumbed tend to enter the crisis of the disease already handicapped by an abnormal prothrombin time. Fluctuations in prothrombin seemed to coordinate in time with fluctuations in sedimentation rate, whole blood specific gravity, and the hematocrit.

Other investigators have also studied alterations in prothrombin and activation of fibrinolysis in an attempt to relate these phenomena to pathological states. Tagnon and his colleagues pointed out that fibrinolysis and a reduction in circulating prothrombin frequently occurs in the serum of patients with shock and burns. Christiansen (6) and Christiansen and McLeod (7) investigated

TABLE III.—PLASMA PROTHROMBIN ALTERATIONS IN SERIES I

Dying Animals

Dog	Death	Pre-operative %	24 hr. %	48 hr. %	72 hr. %	96 hr. %	Fibrinolysis at time of lowest prothrombin
1	25 hrs.	133	60.8	Dead			Negative
2	96 hrs.	143	55.3	133.0	173.0	87.8	Negative
3	48 hrs.	62.4	42.0	58.1	Dead		Negative
14	48 hrs.	163.0	151.0	Dead			Negative
20	50 hrs.	79.6	61.3	41.6	Dead		Negative
21	104 hrs.	78.6	50.6	43.0	48.4	72.7	Negative
23	26 hrs.	141.7	81.3	Dead			Positive
26	72 hrs.	67.2	37.2	45.3	Dead		Negative
28	72 hrs.	70.0	24.7	29.6	Dead		Positive
9	Average prothrombin	104.4	62.7				

Living Animals

15	Lived	100	110	66.0	80		Negative
16	Lived	202.0	180.0	103.0	125.0		Negative
17	Lived	84.7	44.0	48.5			Negative
30	Lived	200.0	71.3	77.0	222.0		Negative
4	Average prothrombin	146.0	101.3				

the activation of an enzyme precursor, present in normal plasma, by filtrates of streptococci, and have proved that this enzyme so activated (activated lysin factor), although proteolytic, is not trypsin. Goodpasture found that specimens of blood from patients with atrophic hepatic cirrhosis possess the property of completely digesting their clot within a few hours at room temperature. Macfarlane's work (16) on fibrinolysis has shown that this phenomenon occurs after surgical operations, exercise, and adrenalin injection.

Since it was our purpose in this portion of the study to evaluate the importance of generalized factors relative to the mortality of the disease, we studied the possible alterations in prothrombin and fibrinolysis as a manifestation of systemic changes of the animal. One other criterion was added, the direct microscopic examination of the liver of the animals. Thus, any direct injury could be detected, even in the event that functional derangement was not reflected.

Fibrinolysis. Prior to surgery and every 24 hours thereafter, until the dog either expired or recovered, plasma fibrinolytic activity was determined. Originally, we used the technique of Kay and Lockwood (12, 13) but found that consistent, similar results were obtained when using 0.5 cubic centimeter of oxalated plasma (1 part 0.1 molar sodium oxalate to 9 parts whole blood) and 0.5 cubic centimeter of 0.025 molar calcium chloride. The latter technique fitted our purpose better because the same reagents were also standardized for use in prothrombin determinations.

Fig. 7. Technique used in measuring fibrinolysis. These tubes contain the fibrin clot of the dogs' plasma and have been incubated for 24 hours. Tube 1 contains 1 drop of saline. No fibrinolysis has occurred. This is a negative determination. Tube 2 contains 3 drops of saline. No fibrinolysis has occurred. This is also a negative determination. Tube 3 contains 1 drop of sac fluid. Partial lysis of the clot has occurred. Tube 4 contains 2 drops of a sac fluid. Partial lysis of the clot has occurred. Tube 5 contains 3 drops of sac fluid. Complete lysis of the clot has occurred. This is a positive determination.

The clot thus formed was placed in a water bath at 37 degrees and observed for 48 hours. Determinations were not made past this period because the possibility of bacterial contamination might alter the interpretation.

If breaking up of the clot (lysis) occurred during this period, it was considered a positive result. If no lysis of the clot occurred it was recorded as negative (Fig. 7).

The 24 dogs used in the control series were studied in this phase of the problem (Table II).

Of the 18 dogs which expired in the control series, only 7 (38.8%) showed fibrinolysis at some period postoperatively and 11 showed no lysis. Of the 7 dogs showing fibrinolysis, 3 showed spontaneous lysis prior to surgery. One other dog displayed spontaneous lysis prior to surgery but showed none postoperatively. These 3 dogs died at an earlier period (37 hours) than the remainder (71.3 hours).

Of the 6 dogs which survived, 1 showed fibrinolysis in the postoperative period.

Prothrombin. Prothrombin determinations were made on 13 of the control animals according to the technique of Tanturi and Banfi.

TABLE IV.—CHLOROFORM TREATED DOGS, PLASMA PROTHROMBIN AND FIBRINOLYSIS, SERIES II DOGS

Fibrinolysis

Dog	Death	Prior to surgery	24 hr.	48 hr.	72 hr.	96 hr.	120 hr.
22	D-32hr.	Positive at 48 hrs.	Negative				
24	D-48hr.	Positive	Positive at 48 hrs.				
27	Lived	Negative	Negative	Negative	Positive	Positive	Positive
31	D-72hr.	Positive at 48 hrs.	Negative	Negative			
33	D-40hr.	Negative	Negative				
37	D-30hr.	Negative	Negative				
38	D-30hr.	Negative	Negative				
43	Lived	Negative	Negative	Negative	Negative		
44	D-24hr.	Negative	Negative				
45	D-52hr.	Negative	Negative	Negative			
10	41 hr.	3	1	0	1		

Prothrombin

Dog	Death	Prior to surgery—%	24 hr. %	48 hr. %	72 hr. %	96 hr. %	120 hr. %
22	D-32hr.	53.8	5.6				
24	D-48hr.	104.3	81.3				
27	Lived	31.2	19.7	26.5	23.2	33.2	50.7
31	D-72hr.	162.7	87.5	63.0			
33	D-40hr.	87.6	56.4				
37	D-30hr.	95.4	78.3				
38	D-30hr.	93.4	77.8				
43	Lived	123.6	79.4	50.6	124.0	64.3	134.0
44	D-24hr.		93.4				
45	D-52hr.		118.0	60.2			
Average	41hr.	94.0	69.7				

Average prothrombin prior to surgery—99.5 per cent in dying animals.
Average prothrombin at 24 hrs.—74.4 per cent in dying animals.
D, death

The prothrombin concentration was reduced postoperatively in all 13 animals (Table III).

Nine of the dogs which expired were in this group of 13 animals. In 2 of these dogs the lowest prothrombin was recorded at 48 hours and 1 of them died at 50 hours. In 7 instances it was lowest at 24 hours and in 3 of the dogs this was a single determination because the animals had expired before 48 hours. However, in 83.3 per cent of the animals studied beyond 48 hours, the lowest prothrombin was not seen at the time of death.

The possible correlation between plasma fibrinolytic activity and hypoprothrombinemia was checked on these 13 animals. In only 2 cases (15.4%) did fibrinolysis occur at the time of lowest prothrombin level recorded.

The average drop in prothrombin at 24 hours was higher in those animals which died (49.8%) than in those which survived (44.7%), but in none of the dogs did the hypoprothrombinemia ever reach hemorrhagic levels.

Liver studies. The third factor studied as a means of determining systemic alterations in the disease was the direct microscopic observation of liver sections taken from dogs dying at various periods postoperatively. Only those animals whose autopsies were per-

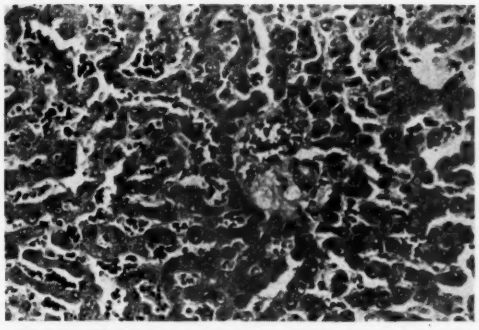


Fig. 8. Photomicrograph of a section taken from the liver of a dog dying of appendicitis with peritonitis at 26 hours. Section removed within 30 minutes of dog's death. No evidence of acute degeneration in liver. Some dilatation of the hepatic sinusoids, with an active congestion is seen.

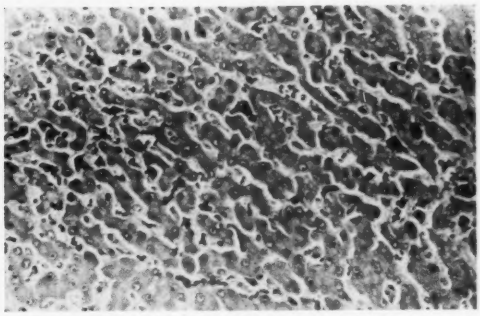


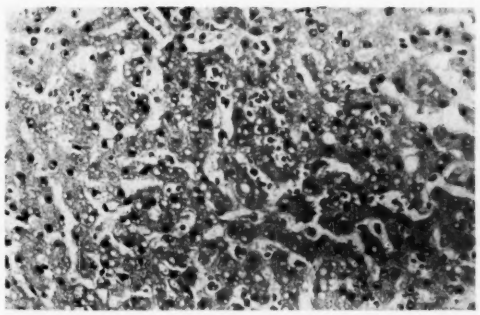
Fig. 9. Photomicrograph of a section taken from the liver of a dog dying of appendicitis with peritonitis at 54 hours. The histological picture of this section differs in no respect from that seen in the section taken from the dog dying at 26 hours.

formed shortly after death were considered. In no case could the amount of liver injury observed be considered as sufficient to cause the death of the animal. The general picture was that of an active congestion, dilatation of the sinusoids, and microvacuolation of the hepatic cells. The nuclei of the cells were normal and no type of acute degenerative process was identified (Figs. 8, 9, 10a and b).

Chloroform intoxication. In an attempt to alter the fibrinolytic-antifibrinolytic equilibrium and prothrombin values in a group of animals at the time of surgery, 15 minutes of intratracheal chloroform was given to 10 dogs immediately following the procedure (series II dogs). This hepatic damage was produced in order to handicap the animals as they entered the crisis of the disease. Thus, early manifestations of derangement of the prothrombin and fibrinolytic values could be expected.

Eight of the 10 animals expired, a mortality of 80 per cent as compared with our control mortality of 75 per cent. However, the average duration of life was 42 hours, as compared with the average of 68 hours in our control series (Table IV).

Spontaneous fibrinolysis was seen prior to surgery in 3 animals, but only one of these showed lysis in the postoperative period and this animal died. The only other animal showing any fibrinolysis in the postoperative period survived. These figures show no significant deviation from those seen in the control animals.



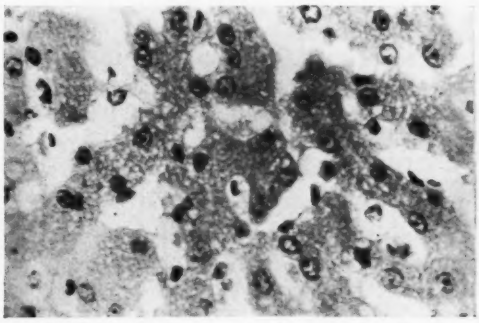
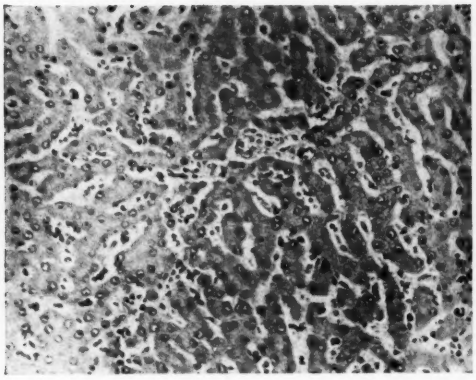


Fig. 10. a, left. Photomicrograph of a section taken from the liver of a dog dying of appendicitis with peritonitis at 104 hours. There is some microvacuolation of the hepatic cells in this section but the general histological picture does not differ from that seen in the liver of dogs dying at an earlier period. b, High power magnification of the same section as Figure 10a. There is no evidence of nuclear change in this section.



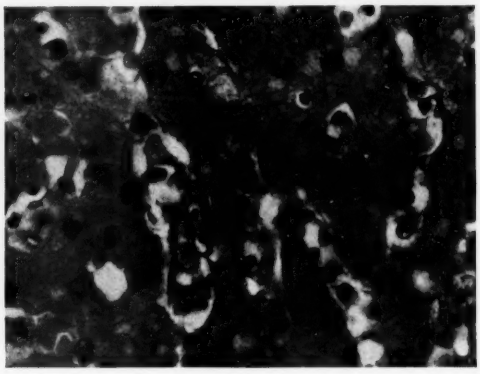


Fig. 11. a, left. Photomicrograph of a section taken from the liver of a dog dying of appendicitis with peritonitis at 30 hours. This dog was subjected to 15 minutes of intratrachial chloroform during the production of the disease. There is no evidence of acute degeneration in this liver. b, High power magnification of the same section as Figure 11a. There is no evidence of nuclear change in this liver.

Twenty-four hours after surgery the average prothrombin level in the dying chloroform treated animals was 74.4 per cent, as compared with a figure of 59.9 per cent in the control group.

It appears that the added effect of chloroform inhalation for 15 minutes to the intoxication of appendicitis does not produce liver injury. As the maximum reduction in prothrombin due to chloroform intoxication in normal animals is reflected at 48 hours, the shorter survival produced by chloroform in the appendiceal peritonitis dogs is due to factors not reflected in variation in prothrombin. The animals die in a period too early for this reflection to be identified.

Liver studies on sections taken from these chloroform treated animals did not differ from the histological picture of the control dogs, since death intervened before any significant necrosis due to the chloroform had occurred (Figs. 11a and b).

LOCAL FACTORS IN EXPERIMENTAL APPENDICEAL PERITONITIS

Among those workers who have stressed the importance of the local gangrenous process in the mortality of this disease, there is no agreement as to what factor, or combination of factors, is of the most importance. In 1938, Bower and his co-workers (1, 10, 11) published several reports on experimental appendicitis in the dog and their conclusions pointed to the organisms of the clostridium group as being of significance. The mortality of the disease was reduced from 74.2 per cent in the control groups to 33.3 per cent in groups which had been given a commercial preparation of gas gangrene antitoxin therapeutically. They were also able to reduce the mortality in pigeons innoculated with Clostridium welchii extracts after they had been given injections of lyophylized convalescent serum of their recovered experimental dogs.

In past years other workers have approached the problem of the cause of death from gangrenous intraperitoneal lesions in a variety of ways. Some claim that a bacterial toxin is the chief offender (21, 22, 27), others place the emphasis on products of protein digestion or tissue autolysis (4, 26). All the investigators have substantial indirect evidence to support their claims.

From the pathological studies on the control animals, one fact remained very consistent. Those animals which were able to wall-off the gangrenous appendix early in the disease process survived, whereas those animals unable to do this at an early period eventually expired. This pointed out the necessity of studying carefully that material, whatever it be, which was produced by the appendiceal appendage as it passed through the stages of necrosis and gangrene. Perhaps

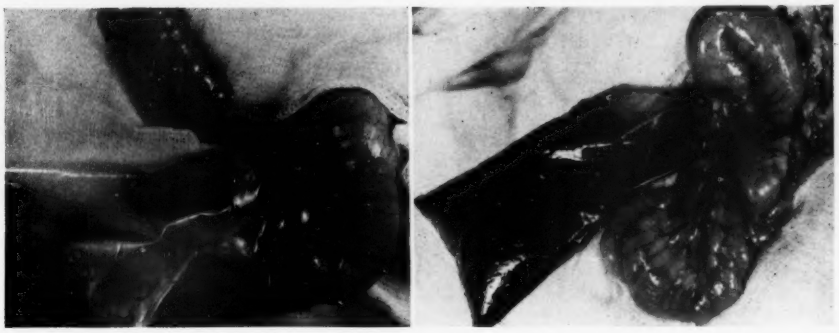


Fig. 12, left. The polythene sac as it is placed over the ligated appendix and sutured to the cecum.
Fig. 13. The same polythene sac as shown in Figure 12, 72 hours later. The dark gangrenous material in the sac was the object of the analysis of local factors associated with appendicitis.

in this material lay the key to an understanding of why some animals could wall-off the appendix and others could present no barrier to the process.

Although the placing of various types of bags over strangulated portions of intestine have been carried out by several workers (1, 14), a new technique was devised by us in order to wall-off artificially the gangrenous appendix and study the material produced in the process. Polythene (polyethylene) sheeting was vulcanized into a small water tight sac, and after ligation of the appendix in the same manner as was done in the control series, this sac was placed over the appendix and sutured snugly to the cecum (Fig. 12). The omentum was then tacked down about the base of this sac in order to prevent any possible leakage. Fifty cubic centimeters of castor oil were given to the dog, exactly as was done in the control group. The dogs were then reoperated upon at appropriate periods. The sac was removed and the gangrenous stump or fecal fistula, whichever the case, was closed with black silk. The omentum was again tacked down over this area. No antibiotics or supportive therapy of any kind were given. The sac fluid was then analyzed according to the technique described below.

This group (series III dogs) consisted of 12 control animals which were reoperated upon at 72 hours. This hour was chosen so as to correspond as closely as was practical with the average life span in our control series. Of the 12 dogs subjected to this procedure, 1 died prior to the second operation presenting a mortality of only 8.3 per cent.

Among the 11 animals which underwent the second procedure, there were no postoperative deaths. Thus, 11 of 12 animals were saved by the simple expedient of artificially walling-off the local inflammatory process.

None of the dogs with the sac-covered, gangrenous appendix which had undergone the second procedure showed any evidence of generalized peritonitis. The sac, however, invariably contained from 25 to 50 cubic centimeters of dark, hemolytic, foul-smelling fluid along with the slimy, necrotic appendix (Fig. 13). In most cases a substantial layer of fibrin had been laid down about the suture line at the base of the sac. Occasionally, the omentum appeared friable near its proximity to the suture line.

The fluid contained in the sac was measured into a series of centrifuge tubes and turned at 1500 r.p.m. for about 10 minutes to remove most of the particulate matter. The supernatant fluid was then passed through a Seitz filter, and the bacteria-free residue was the object of our investigation.

Fibrinolysis. Since it was not our purpose in this phase of the experiment to repeat any controversial work in order to add further evidence to one side or the other, we approached the analysis of this fluid from another direction. Our investigations had shown that the production of fibrin about the local area

TABLE V.—SAC FLUID AND ABDOMINAL EXUDATE DETERMINATIONS

Series III Polythene Sac Dogs

Dog	Outcome of operation	Fibrinolysis		Hyaluronidase	Lecithinase
		Plasma	Sac		
54	Lived	Negative	3 plus		
56	Lived	Negative	Negative		
57	Lived	Partial	3 plus		
59	Lived	Negative	3 plus		
60	Lived	Negative	Negative		
62	Lived	Negative	3 plus	5 plus	Negative
63	Lived	Negative	1 plus	5 plus	Negative
65	Lived	Negative	2 plus	4 plus	Negative
66	Lived	Negative	3 plus	1 plus	Negative
67	Died		3 plus	5 plus	Negative
69	Lived	Negative	2 plus	5 plus	Negative

Series IV Plain Appendicitis—Reoperated Dogs

Dog	Time and outcome of second operation	Fibrinolysis		Hyaluronidase	Lecithinase
		Plasma	Abdominal fluid		
68	24 hr. Recovered	Negative	Negative	Negative	Negative
70	24 hr. Recovered	Negative	Positive	3 plus	Negative
71	44 hr. Died		Negative	4 plus	Negative
72	44 hr. Died	Negative	Negative	4 plus	Negative
73	48 hr. Died	Negative	1 plus	Negative	Negative
74	48 hr. Died		1 plus	Negative	Negative
75	42 hr. Died	Negative	Negative	Negative	Negative
76	43 hr. Died		Negative	Negative	Negative
77	43 hr. Died		1 plus	Negative	Negative
78	44 hr. Died	Negative	Negative	Negative	Negative
79	30 hr. Died	Negative	3 plus	Negative	Negative

was one of the important factors associated with ability to wall-off the gangrenous appendix. The inability of the animal to present a fibrin barrier, or the dissolution of any fibrin produced about the gangrenous appendix, meant certain death for the dog. Our first analysis, therefore, involved the attempt to identify the presence of a fibrinolysin in the local fluid.

The method of detecting an activator of the lysin factor involved setting up a series of 3 tubes for each animal.

Tube 1—0.5 cubic centimeter of plasma plus 0.5 cubic centimeter of calcium chloride plus 3 drops of saline

Tube 2—0.5 cubic centimeter of plasma plus 0.5 cubic centimeter of calcium chloride plus 1 drop sac fluid, plus 2 drops saline

Tube 3—0.5 cubic centimeter of plasma plus 0.5 cubic centimeter of calcium chloride plus 3 drops sac fluid

These were incubated for 24 hours and lysis was recorded as follows: lysis in Tube 2 equals 2 plus, lysis in both tubes equals 3 plus, partial lysis in either tube equals 1 plus. Lysis in control tubes was also noted, but in every case this corresponded with the activity of the dog's serum at the time of surgery (Fig. 7).

Eleven animals were studied in this way (Table V). Eight (72.7%) showed lysis in one or both tubes; 1 (9.1%) showed only partial lysis; and 2 (18.1%) showed no lysis. Only 1 of the dogs in this series of 11 showed partial lysis in the plasma at the time the sac was removed.

Samples of peritoneal exudate from 11 dogs in a plain appendicitis series which had been reoperated upon at various periods following production of the disease (series IV) were also studied for fibrinolysis. Six of these fluids showed no fibrinolysis, 4 showed partial lysis, and 1 showed complete lysis of the clot. The plasma of none of the animals showed spontaneous lysis in the control tube (Table V).

Hyaluronidase. The basis for our second analysis arose from a study of the pathogenesis of the local process. Unless the animal can naturally wall-off the area of gangrenous appendix early in the disease, a steady progression of events takes place which eventually ends in the death of the animal. This would indicate that some product relentlessly breaks down all natural barriers once it is present in sufficient amounts. Such a spreading factor has been identified in many types of infection (5, 8), and recently (11, 17) the enzyme hyaluronidase has been named as one of the chief components of this spreading factor in streptococcus, staphylococcus, and clostrid-

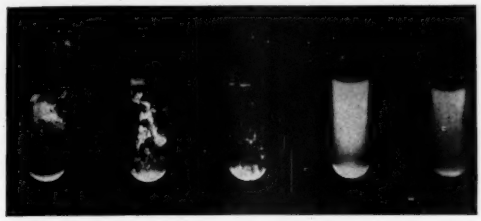


Fig. 14. The mucin clot prevention method of determining presence of hyaluronidase. Increasing amounts of the exudate from .031 cubic centimeter in tube 1 to 0.5 cubic centimeter in tube 5 have been added to the potassium hyaluronate solutions and incubated 20 minutes. The absence of the mucin clot in the tubes of higher concentration of the exudate indicates that digestion by the enzyme has occurred.

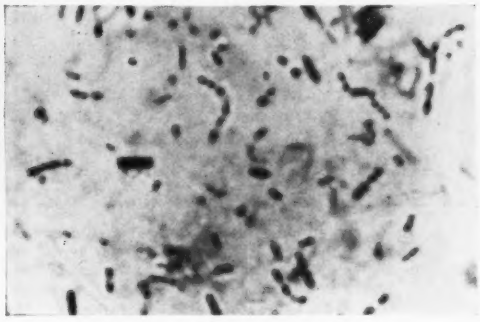


Fig. 15. Photomicrograph of a smear taken from the sac fluid at 72 hours and stained by the Gram technique.

ium infections. The identification of this enzyme in the products of a gangrenous appendix was, therefore, the object of the second analysis.

Hyaluronidase determinations were done by mucin clot prevention method of McClean (18) serial dilutions of the material from 1:2 to 1:32 in 5 tubes being used. Values were recorded as units corresponding to the number of the tube of highest dilution in which the enzyme appeared, 5 being the highest figure (Fig. 14).

The sac fluid from 6 dogs was studied in this phase of the work. All of the fluid contained the enzyme, 5 (83.3%) of them in amounts detectable in .031 cubic centimeter of the exudate (Table V).

To compare the amount of hyaluronidase present in the localized process with that found in the abdominal cavity during generalized peritonitis, samples of exudate from dogs in series IV (plain appendicitis reoperated upon) were studied for the enzyme. Eleven such exudates were analyzed and in only 3 cases was any enzyme detected. These figures are stated in Table V.

Lecithinase. Our third investigation was undertaken because of our interpretation of the clinical picture and pathological state in the dying animals, plus the examination of smears taken from the gangrenous exudate. The tachycardia, hyperpnea, and weakness seen in the moribund animals plus the severe, hemolytic type of peritonitis, the slimy gangrenous omentum and presence of gas in the peritoneal cavity combined with the presence in almost every instance of a gram positive rod-shaped bacillus on smears (Fig. 15) led us to the belief that a toxin, probably that elaborated by one of the anaerobic bacilli, was of significant importance.

Although many workers have been in accord with this theory, their evidence has been based on observations dependent on the protection of small animals with commercial or prepared gas gangrene antitoxin before or after the gangrenous material had been injected. Such a technique, although very accurately and skillfully done, presents many variables which may alter the evidence and is, in a fundamental sense, only indirect proof of the existence of a specific toxin.

In order to avoid these factors, our experiment was aimed at a direct titration of the toxin of Clostridium welchii from the gangrenous material. Recently, several workers (15, 25) have identified the enzyme lecithinase as being the lethal toxin (alpha toxin) of the type A-Clostridium welchii organism. Our third analysis, therefore, was an attempt directly to identify this toxin in the gangrenous material.

McClean's original technique for the detection of the toxin of Clostridium welchii (18) was modified somewhat by us and applied to the study of the appendiceal exudate. This procedure is based on the ability of lecithinase to produce a turbidity in a dilute egg yolk solution in the presence of calcium ions and is very specific and sensitive. Control tubes

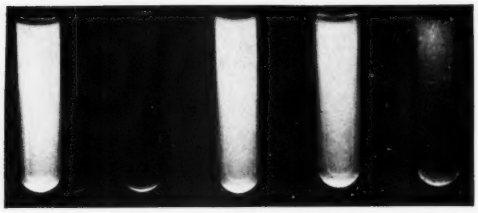


Fig. 16. Technique used in lecithinase determinations. These tubes have been incubated for 2 hours at 37 degrees Centigrade. Tube 1 contains 0.5 cubic centimeter of sac fluid. Turbidity is evident, proving the presence of clostridium toxin. Tube 2 contains 0.5 cubic centimeter of sac fluid plus 1.0 cubic centimeter of convalescent dog serum. No turbidity is seen, indicating that this serum inhibits the toxin. Tube 3 contains 0.5 cubic centimeter of sac fluid plus 1.0 cubic centimeter of commercial polyvalent gas gangrene antitoxin. Turbidity is seen, indicating that this type of antiserum does not inhibit the toxin produced in the dog. Tube 4 contains 6 minimum lethal doses of Clostridium welchii toxin. Turbidity is apparent. Tube 5 contains 6 minimum lethal doses of Clostridium welchii toxin plus 1.0 cubic centimeter of commercial polyvalent gas gangrene antitoxin. No turbidity is seen, indicating that this antitoxin inhibits the commercially prepared toxin.

were set up with antitoxin and comparisons were made on a Coleman universal spectrophotometer using a monochromatic beam of 560 gamma.

Six sac fluids and 11 samples of peritoneal exudate in generalized peritonitis (series IV dogs) were analyzed in the original experiment. Standard polyvalent gas gangrene antitoxin was employed for the control standard in each of these experiments. Although turbidity appeared in several of these analyses, the turbidimetric differences recorded in the control and unknown tubes was of no significance, therefore, we assumed that this turbidity was a constant factor and our results were recorded as negative in all 17 determinations (Table V).

Since several dogs which had recovered from the experimental diseases were available for further study, it was decided to titrate the antitoxic properties of their serum against the exudate and compare these results with those obtained with the commercial gas-gangrene antitoxin.

The results in this experiment were quite different. It was found that although the commercial antitoxin had little or no effect in preventing turbidity, our dogs' convalescent serum inhibited the toxin to such an extent that significant spectrophotometric differences were recorded (Fig. 16).

Experimental appendicitis was then produced in another series of 16 dogs (series V). Polythene sacs were placed over the ligated appendix in 10 of these animals. One of these dogs died of pneumonia within 24 hours of the first procedure and was therefore discounted. Only 1 of the 9 animals subjected to the second procedure died.

The toxin of clostridium was identified in 8 of the 9 sac fluids analyzed (88.8%) and the average turbidimetric reading was 69.1 per cent. Hyaluronidase was found in every fluid analyzed and in 5 instances (55.5%) was detected in less than .031 cubic centimeter. Streptokinase appeared in significant concentrations in 7 of the 9 sac fluids (77.7%). These figures are recorded in Table VI.

The general peritoneal exudate in 6 dogs of this series was also analyzed. Lecithinase was detected in 5 of the 6 animals (83.3%) and the average turbidimetric reading was 71 per cent. Hyaluronidase was detected in only 3 fluids. Of 5 exudates studied for fibrinolysin, 3 contained the enzyme in small amounts (Table VI).

Histamine studies. In an effort to evaluate the role of histamine shock as a factor in the death of the experimental animal and to compare the relative toxicity of sac fluid and known Clostridium welchii toxin, several dogs were subjected to injections of these fluids.

The general peritoneal exudate from 8 dogs with appendicitis was analyzed as to its histamine content, isolated guinea pigs' gut being used as a method of assay. Only one fluid of this group was shown to contain any appreciable amount of histamine or histamine-like substances.

Random samples of two of these fluids containing minimal amounts of histamine were then injected intravenously into 2 dogs and histamine release into the dogs plasma was assayed. A significant release was observed in both animals.

Two animals were then selected for injections of Clostridium welchii alpha toxin intravenously. Histamine release was studied. No significant increase in plasma histamine was

TABLE VI.—PERITONEAL AND SAC FLUID DETERMINATIONS, SERIES V DOGS

A. Peritoneal exudate

Dog	Time	Fibrinolysis		Hyaluronidase	Lecithinase %	Outcome
		Plasma	Exudate			
80	30 hr.		1 plus	5 plus	28	Died
82	30 hr.	1 plus	1 plus	3 plus	83	Survived
84	43 hr.	Negative	Negative	0	0	Sacrificed
85	22 hr.	Negative	1 plus	0	68	Sacrificed
86	48 hr.	Negative	Negative	0	92	Sacrificed
87	48 hr.			3 plus	84	Sacrificed

B. Sac fluid

Dog	Time	Fibrinolysis		Hyaluronidase	Lecithinase %	Outcome
		Plasma	Exudate			
81	48 hr.	Negative	1 plus	5 plus	39	Survived
83	72 hr.	Negative	1 plus	4 plus	42	Survived
88	72 hr.	Negative	2 plus	3 plus	0	Died in 24 hrs.
89	72 hr.	Partial	3 plus	3 plus	76	Survived
90	72 hr.	Negative	3 plus	5 plus	91	Survived
91	72 hr.	Negative	3 plus	5 plus	81	Survived
92	48 hr.	Partial	3 plus	5 plus	55	Survived
93	Pneumonia—Died in less than 24 hr.					
94	30 hr.	Negative	3 plus	5 plus	77	Survived
95	24 hr.	Negative	2 plus	4 plus	92	Survived

found in either case. In one of these animals careful blood studies were carried out. Blood was drawn from the heart just before the animal died. This blood failed to show any lysis in 48 hours. Prothrombin level at death was decreased, but this decrease was due to actual liver injury, as titration of the plasma against protamine showed no heparin release. Similar studies on a dog injected with sac fluid have shown lysis to occur and decrease in prothrombin in presence of heparin release.

Control studies on standard Clostridium welchii toxin and samples of fecal matter were carried out in order to evaluate the results of this experiment. No variation in these control analyses could be held responsible for the results in the experimental animals (Table VII).

TABLE VII.—CONTROL STUDIES ON FECAL SUSPENSIONS PREPARED FROM RANDOM SAMPLES OF DOG FECAL MATTER

Lecithinase

Fecal suspension	Result	
1	Negative	
2	Negative	
3	Negative	
4	Negative	
5	Negative	
6	Negative	

Hyaluronidase

Fecal suspension	Result	Amount detected	
1	Negative		
2	Negative		
3	Positive	0.25 cc. (2 plus)	
4	Positive	0.20 cc. (2 plus)	
5	Negative		
6	Negative		
7	Negative		
8	Negative		
9	Positive	0.063 cc. (4 plus)	
10	Negative		

Fibrinolysis

Fecal suspension	Control 3 drops saline	1 Drop fecal suspension	3 Drops fecal suspension
1	Negative	Negative	Negative
2	Negative	Negative	Partial
3	Negative	Negative	Partial
4	Negative	Negative	Negative
5	Negative	Partial	Complete
6	Negative	Negative	Negative
7	Partial	Negative	Partial
8	Negative	Negative	Negative
9	Negative	Negative	Partial
10	Negative	Negative	Negative

DISCUSSION

Although the wide clinical use of the sulfonamides and antibiotic drugs has reduced the annual mortality of appendicitis and peritonitis to less than 4 deaths in 100,000, a basic knowledge of the pathogenesis of this disease is an essential aid to the surgeon. The indiscriminate use of these powerful weapons will never supplant sound surgical judgment based on a true understanding of the disease mechanism.

The complexity of factors associated with this disease has warranted considerable ex-

perimental work, and from this work has come a vast amount of knowledge concerning alterations in many of the physiological mechanisms of the experimental animal. Our present study has been undertaken in an effort to direct the attention of both the clinical and research surgeons to those factors which we believe are the most significant in the morbid process of appendicitis and peritonitis.

The systemic alterations seen in our experimental animals did not appear to be either of a severe enough degree, or consistently present, to designate such derangements as fundamental mechanisms in the morbid process.

The decrease in prothrombin seen in every animal postoperatively certainly points out some degree of liver injury. The greatest drop appeared in 24 hours in 55.5 per cent of the dying animals and in only 44.4 per cent of the animals did the lowest prothrombin concentration appear near the time of death. From these figures it cannot be said that alteration in prothrombin concentration is a predisposing factor in the death mechanism. It is more likely that a mild degree of liver injury manifested by prothrombin decrease is a reflection of some primary etiological factor.

There was no correlation between plasma fibrinolysis and death in our animals. Only 38.8 per cent of the dying animals showed any fibrinolysis postoperatively and 16.6 per cent of the living animals also displayed this phenomenon. The importance of such a factor necessarily must be secondary when its presence is identified in less than one-half of the dying animals.

The small percentage of animals (15.4%) showing fibrinolysis at the time of the lowest prothrombin level does not substantiate the theory that fibrinolytic enzymes in the blood destroy circulating prothrombin.

Microscopic examination of the liver in dying animals gave us no indication that hepatic damage could account for death. Nuclear disintegration or parenchymal injury were absent or minimal in every specimen studied. The congestion, dilatation of the sinusoids and microvacuolation, however, could very well be the response to a generalized toxemia. This amount of hepatic cellular damage probably accounts for the decrease in circulating prothrombin, but cannot be held responsible for the mortality.

The earlier death in that group of animals subjected to chloroform intoxication cannot be attributed to any alteration in fibrinolytic antifibrinolytic equilibrium, or decrease in circulating prothrombin, since these phenomena were not in evidence at the time of the animals' deaths. Perhaps some synergistic action of the liposolvent properties of chloroform and lecithinase tend rapidly to overcome the natural defense of the animal. This question bears further investigation.

The importance of the local factors as initiating mechanisms for the production of death is emphasized since recovery can be obtained in more than 90 per cent of animals by artificially walling-off the local gangrenous process. In the natural course of the disease process, the animal would be faced with the problem of combating those factors which we have studied, thus the local area of gangrene assumes the importance of a battle ground on which the invasive forces and natural body defenses strive for survival or death.

The invasive and lethal properties of the local exudate are probably dependent on the synergy of the bacterial flora of the bowel when a suitable medium for growth is presented, namely, the gangrenous appendix. Synergism of the bacteria, we believe, is necessary for proper metabolic processes which eventuate in an increased toxicity of the local fluid (19).

The identification of an activator of the lysin factor in 80 per cent of the sac fluids suggests that this element of the local process may be significant. This enzyme is probably a product of streptococcal growth, streptokinase, and its ability to produce fibrinolytic properties in the local exudate indicates that a natural walling-off of the area by deposition of fibrin, may be a difficult thing for the host to accomplish. Then, too, the experimental studies of Grob have demonstrated that the products of protein digestion, present when fibrinolysis occurs, in addition to inhibiting the bacteriostatic action of sulfa drugs, also directly promotes bacterial growth. This fact may account not only for the inability of 75

per cent of our animals to wall-off the local lesion, but may also explain why the 4 animals in our control series showing spontaneous lysis prior to surgery, died at an earlier hour than the remainder of the control dogs. Thus, the presence of plasma fibrinolysis, or digestion of local fibrin, about a gangrenous intraperitoneal lesion would hasten the disease process simply because of a more suitable environment for bacterial growth.

The mucolytic properties of hyaluronidase must also tax the defense mechanisms in the peritoneal cavity. This enzyme has been identified in cultures of streptococci, staphylococci, and Clostridium welchii organisms, but regardless of its origin from the necrotic appendix, its presence in significant amounts in 83 per cent of the sac fluids indicates that such a spreading factor must play an integral role in the pathological mechanism.

The direct identification of the toxin of clostridium from 89 per cent of the exudates analyzed, very strongly suggests that this enzyme may play a vital part in the morbid process. No attempt was made by us to determine concentrations of this toxin, except by general spectrophotometer readings. The inability of commercial gas gangrene antitoxin to neutralize its lipolytic property and the high degree of inhibition from serum of convalescent dogs point out the likelihood that the anaerobic organisms harbored by the dog are of a different species than those in man. This fact would question the results of workers who have endeavored to prove the absence of clostridium toxins in intraperitoneal infections by protective properties of commercial gas gangrene antitoxin on laboratory animals.

The presence of lecithinase in the early stages of the disease is compatible with the clinical picture of progressive lethargy and toxemia due to irreversible changes of the lipo-protein structure of the cell membrane, especially of the nervous system and other vital organs.

The comparison of blood studies and fluid assays have convinced us that the injection of sac fluid, or abdominal exudate, kills the animal by peptone shock before the toxic effect of the lecithinase is manifested. Then, too, the single injection of a specified amount of toxin cannot simulate the constant production occurring in an intraperitoneal infection.

The relatively smaller amounts of all three factors—fibrinolysin, hyaluronidase and lecithinase—identified in the peritoneal exudate of peritonitis as compared to the sac fluid, may indicate either the presence of some antienzyme properties in the peritoneal cavity similar to that seen in the dog's serum, or the fixation of the enzyme in the body tissue once the infection has been initiated.

The absence of lecithinase and minimal concentration of hyaluronidase and streptokinase in the fecal matter of normal animals indicates that their appearance in the appendiceal exudate is dependent on a medium such as is present in gangrenous appendicitis. There is every reason to believe that the same enzyme systems will play a role in the production of peritonitis in any necrotic intraperitoneal lesion for example, loop obstructions, or incarcerations of the bowel.

CONCLUSIONS

1. Experimental appendiceal peritonitis in the dog is a disease in which the local release of bacterial enzymes and toxins from the gangrenous appendage is of more significance in the morbid process than any alteration of circulating prothrombin or derangement of fibrinolytic-antifibrinolytic equilibrium in the circulating blood.

2. Ninety-two per cent of dogs will recover from this disease when a simple polythene sac is placed over the ligated appendix and the gangrenous exudate removed in 72 hours. Removing the gangrenous appendix at 48 hours when no sac has been placed over it eventuates in 100 per cent mortality after the second procedure. This points to the local area as of basic importance and early surgical removal of this focus should be the fundamental rule in surgical treatment of the disease.

3. The inability of 75 per cent of a control series naturally to wall-off the gangrenous appendix is probably dependent on the action of two bacterial enzymes identified in the gangrenous exudate. Streptokinase prevents fibrin deposition about the necrotic appendage by its lysing effect on this protective barrier.

Hyaluronidase provides a mucolytic and a spreading factor which makes possible the dissemination of bacteria into the general peritoneal cavity.

4. Lecithinase, the lethal factor of the alpha toxin of Clostridium welchii has been identified in 89 per cent of the gangrenous appendiceal fluids. This enzyme produces a severe toxemia by its absorption into the general circulation.

5. The inability of commercial gas gangrene antitoxin to inhibit the lecithinase produced by the clostridium of the dog has been demonstrated. Serum of convalescent dogs, or of dogs which have been inoculated with their own fecal matter, does inhibit the splitting of lecithin.

6. Although no single factor can account for the death from peritonitis, the lethal toxin of Clostridium welchii can be held primarily responsible for the alterations in hemodynamics, hepatic functions, and metabolic status seen in the course of the disease. These changes are systemic reflections of the local disease mechanisms, and although contributory to the eventual death do not represent the essential factors in the pathogenic picture.

7. The action of the sulfonamides and the antibiotics in aborting the disease process is probably dependent on destroying certain bacteria present in the exudate, thus preventing a synergistic growth necessary for the production of metabolites needed for lethal enzyme production.

8. Histamine studies before and after injection of sac fluid indicate that death from this type of experimentation results from peptone-like shock before any toxemia from the lecithinase present can become manifested.

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BLOOD AND "AVAILABLE FLUID" (THIOCYANATE) VOLUME STUDIES IN SURGICAL PATIENTS

Part II. Operative and Postoperative Blood Loss with Particular Emphasis Upon Uncompensated Red Cell Loss

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IT is the responsibility of the surgeon to know the amount of blood a patient may lose as a result of an operative procedure. Studies of blood loss reported in the literature (1, 3, 13, 21, 22, 23, 25, 33–36) have been made by colorimetric or gravimetric measurement of the blood removed from the wound on towels and sponges and in the irrigating fluid during the operation. Such studies have led to the compilation of tables of average operative blood loss for different procedures (3, 5). It is the purpose of the present report to suggest that these figures may have given surgeons an unwarranted sense of security for two reasons: (1) the amount of blood removed from the wound at the time of operation may not represent the actual amount of blood lost to the circulation, and (2) postoperative blood loss may occur in amounts greater than the actual operative blood loss. This loss not infrequently results in uncompensated red cell loss.

In previous studies (12, 19) from this laboratory describing serial changes in the blood volume and available fluid in the postoperative surgical patient, large decreases in the postoperative red cell volume and hematocrit were not infrequently noted. These were of sufficient magnitude to lead us to question whether they could be accounted for by operative blood loss. Thomas, Adams, and Thornton, also utilizing the blood volume method in 5 patients undergoing thoracic surgery, likewise noted decreases in the red cell volume even when adequate amounts of blood had been given by transfusion to replace the blood removed from the wound at operation. Thornton, Adams, and Schaefer and Lord and Hinton have noted that large amounts of plasma and red cells may be lost from and into the chest postoperatively. That the postoperative decreases in the red cell volume noted in this laboratory and by others might be accounted for by postoperative blood loss was deemed probable. It seemed desirable to reinvestigate the problem of blood loss, both that occurring during, as well as following, various operative procedures.

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MATERIAL AND METHODS

The subjects of this study were a group of patients from the ward and private surgical services of the Massachusetts Memorial Hospitals.

Blood loss at operation. (a) Gravimetric method. Gravimetric determinations of the blood lost in the packs and sponges were carried out according to the method described by Wangensteen. Where possible double layers of packs were sewed to the margin of the wound to prevent blood being absorbed on the drapes or towels. Blood on the gloves and instruments was removed as rapidly as accumulated by dry sponges. No saline irrigations or wet packs were used whenever this was feasible. When large walling off packs were moistened with saline they were discarded. The scales which were used in the weighing process read to an accuracy of 0.1 gram.

(b) Colorimetric method. The colorimetric determinations reported here were based on

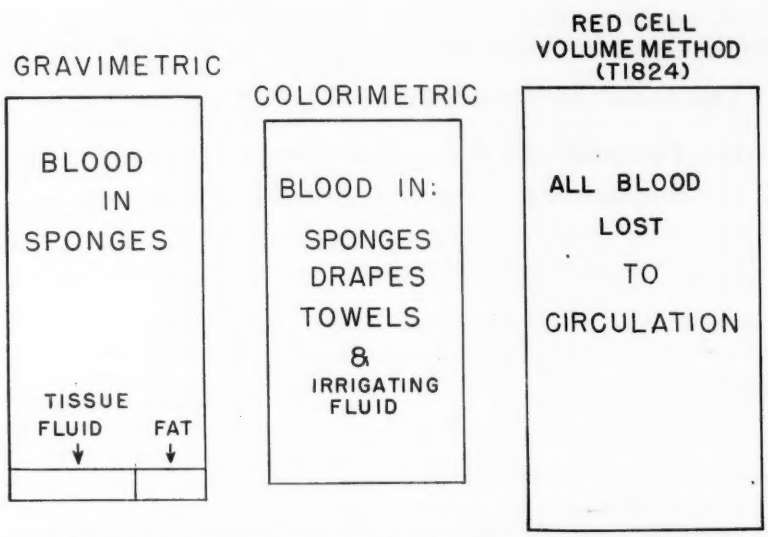

Fig. 1. Graphic representation of results of three methods of studying blood loss at operation.

a procedure modified from the acid hematin method of Gatch and Little. Oxyhemoglobin determinations were carried out on the Coleman junior spectrophotometer(2). A sample of 5 cubic centimeters of the patient's blood drawn preoperatively was diluted to 1000 cubic centimeters with distilled water and, upon being cleared with dilute ammonium hydroxide and filtered, was read on the log scale at a wave length of 540 millimicrons against distilled water. Properly diluted samples of the hemoglobin extracted from the sponges and towels were treated and read in the same fashion. With corrections for dilution the amount of blood lost was calculated by the following modification of the Lambert Beer law for spectrophotometric differences in optical density.

$$C_2=\frac{C_1}{D_1}\times D_2$$ where C_2 = concentration of unknown, C_1 = concentration of standard, D_1 = optical density of standard, D_2 = optical density of the unknown

(c) Red cell volume method. In all cases serial blood volume studies were carried out in the preoperative and postoperative periods as detailed in the first paper of this series (19). Total blood volume and red cell volume were determined from the plasma volume and hematocrit (14). In this paper all references to red cell volume refer to the red cell volume as determined by this method. All measurements of plasma volume were carried out in the basal postabsorptive state with the patient resting supine in bed for at least 2 hours prior to the test.

On experimental grounds (11, 15, 29) the objection may be raised that the red cell volume as measured by this method is about 15 per cent higher than the absolute red cell volume. Nonetheless, the same error is present in all determinations both preoperatively and postoperatively so that repeated determinations in the same patient should yield reliable information as to red cells lost or gained by the circulation.

In selected cases the plasma volume was determined in the preoperative and immediate postoperative periods. Since the plasma volume may change relatively rapidly in response to intravenous infusions or acute severe blood loss and thus alter the total blood volume, neither plasma volume nor total blood volume changes can be used as a reliable index of

TABLE I.—BLOOD LOSS AT OPERATION IN 20 CASES, DETERMINED BY COLORIMETRIC OR GRAVIMETRIC METHODS.

Case	Age	Sex	Operation	Operative blood loss c.c.	
1	56	M	Subtotal gastrectomy	480*	
2	52	M	Subtotal gastrectomy	100	
3	50	M	Exploratory thoracotomy	1600	
4	36	M	Thoracotomy and lingulectomy	650	
5	50	M	Exploratory thoracotomy	450	
6	38	M	Transthoracic vagotomy	250*	
7	52	M	Cholecystectomy, exploration of common bile duct, appendectomy	185*	
8	45	F	Cholecystectomy, exploration of common bile duct, appendectomy	195*	
9	42	F	Subtotal thyroidectomy	143*	
10	50	F	Hysterectomy	445*	
11	42	M	Hernioplasty	152*	
12	17	M	Hernioplasty	92*	
13	66	M	Transurethral prostatectomy	193	
14	68	M	Transurethral prostatectomy	110	
15	59	M	Total cystectomy with implantation of ureters into colon (one stage)	477	
16	40	M	Lumbodorsal splanchnicectomy	310*	Range 105-310 Av. 201 cc.
17	39	M	Lumbodorsal splanchnicectomy	140*	
18	32	M	Lumbodorsal splanchnicectomy	167*	
19	38	M	Lumbodorsal splanchnicectomy	285	
20	40	M	Lumbodorsal splanchnicectomy	105*	

*Gravimetric determinations.

blood loss. Because the total red cell volume is resistant to changes resulting from hydrating or dehydrating procedures, this fraction of the blood volume was used to compute the amount of blood lost from the circulation as a consequence of the operative procedure. Similarly, postoperative blood loss was computed from the successive postoperative red cell volumes. In this manner blood lost at operation and blood lost postoperatively could be individually assayed.

RESULTS—OPERATIVE BLOOD LOSS

Table I illustrates the blood loss at operation in a series of 20 patients as determined

Blood on sponges
Blood on drapes
Blood on towels
Blood on gloves
Blood on gowns
Blood on instruments
Blood in surgical specimen
Blood in wound not absorbed by sponges
Blood lost to circulation through ligatures e. g.

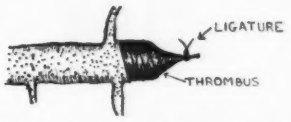

Fig. 2. Details of sources of loss measured by the red cell volume (T1824) method of studying operative blood loss.

by the usual gravimetric or colorimetric methods. Although this series is relatively small the values for operative blood loss as measured by the classical methods do not differ significantly from those reported for comparable procedures in the literature. The operative blood loss in 5 cases undergoing lumbodorsal splanchnicectomy as described by Smithwick averaged 201 cubic centimeters at each stage.

The colorimetric method of determining blood loss contains a source of error in that it is based on hemoglobin determinations. Even using the photoelectric colorimeter Evelyn has reported an error of $\pm$ 2 per cent. More important than this are multiple other errors introduced by incomplete extraction of the hemoglobin from the sponges, by contamination of sponges with bile or iodine, and errors in the process of dilution which though small may greatly alter the final value.

In comparing the colorimetric and gravimetric methods for the measurement of the blood removed from the wound the gravimetric procedure yielded the more reliable results. However, this method also is subject to certain errors. Baronofsky and associates noted that small increments in weight may be due to tissue fluid absorbed by the sponge. In our experience with colorimetric studies on material which had previously been measured gravimetrically we were repeatedly impressed

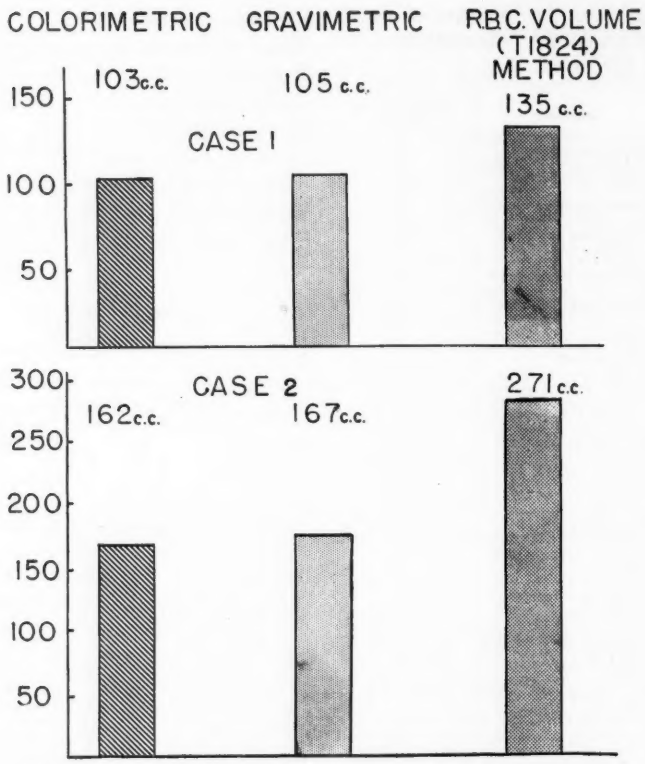

Fig. 3. Comparison of operative blood loss as studied by the colorimetric, gravimetric, and red cell volume methods in 2 cases.

by the heavy layer of fat that rose to the top during the extraction process. This may be of importance in carrying out gravimetric blood loss studies in the obese patients in whom extensive dissection is carried out through fatty layers.

The question of errors due to evaporation also was investigated. In 4 experiments where 50 cubic centimeters of blood was placed on sponges and exposed to the air in the laboratory for 1 hour, the loss of weight by evaporation of water averaged 2.88 grams. Thus, it may be assumed that in the operating room which maintains a relatively high humidity, errors from loss of weight by evaporation will be kept at a minimum if sponges are weighed within 15 minutes of the time of discard from the table.

In contrast to the colorimetric and gravimetric methods, the red cell volume method, based on the principle of dilution of injected dye, measures the total volume of blood in the circulation. Inasmuch as there are no significant storehouses of red cells in the human body, serial measurements by this method reveal the total amounts of blood lost from the circulation as a result of the operative procedure (Figs. 1, 2). This includes not only the blood removed from the wound, but in addition, all blood lost in the surgical specimen, infiltrated into the wound and surrounding tissue spaces and not absorbed by sponges, or immobilized in vessels proximal to ligatures. It is evident that this method should yield higher values for the amount of blood lost that can be measured by either the color-

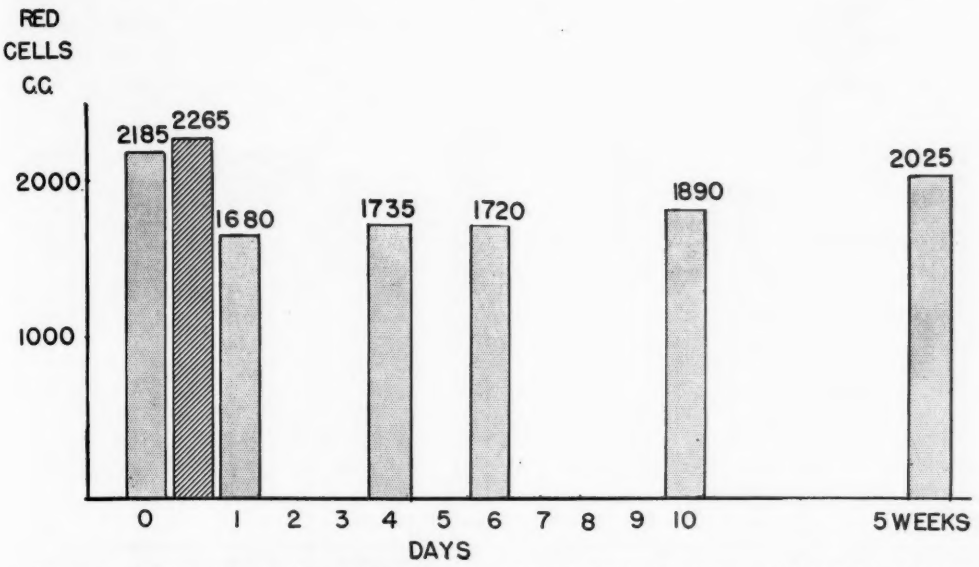

Fig. 4. Thoracotomy with resection of lingular bronchus; postoperative blood loss, 1200 cubic centimeters. The difference between actual and theoretical red cell volumes on first postoperative day is 585 cubic centimeters of red cells or 1280 cubic centimeters of whole blood. Theoretical red cell volume, which is indicated by the diagonally lined column, was computed in the manner which is described in the text. Note that the red cell volume has not returned to the preoperative levels at the end of 5 weeks' time.

imetric or gravimetric methods which measure only the blood removed from the wound on the sponges and towels.

Figure 3 represents a comparison of the three methods of studying blood loss in 2 cases. In both instances there was close agreement between the colorimetric and gravimetric methods which measure only the blood removed from the wound. The red cell volume method, which measures the blood lost to the circulation, yielded significantly higher values.

The method is particularly satisfactory where large amounts of blood are lost. It is useful both in measuring progressive loss and total depletions of the red cell volume and in evaluating replacement therapy. The chief difficulty with the red cell volume method is that it requires special apparatus and meticulous technique. While yielding satisfactory results as a clinical research method, it is at the present time too difficult technically to be considered practical for routine clinical use.

RESULTS—POSTOPERATIVE BLOOD LOSS

The red cell volumes studied serially in 4 cases at various intervals during the preoperative and postoperative periods are illustrated in Figures 4, 5, 6, and 7. It will be observed in Figures 4, 6, and 7 that striking diminutions in the red cell volume occurred. Blood loss at operation was studied in all cases by the gravimetric and colorimetric methods. On the basis of the total blood loss at operation multiplied by the preoperative hematocrit, the number of cubic centimeters of red cells lost at operation was computed.

The lightly stippled areas in each figure represent the actual red cell volume. The heavily lined column in each figure represents the theoretical red cell volume, i. e. the preoperative red cell volume (at 0 day) plus the red cell gain by transfusion and minus the red cell loss at operation computed from the colorimetric or gravimetric operative blood loss and the hematocrit. More specifically, in each case the theoretical red cell volume represents that which should have been present if

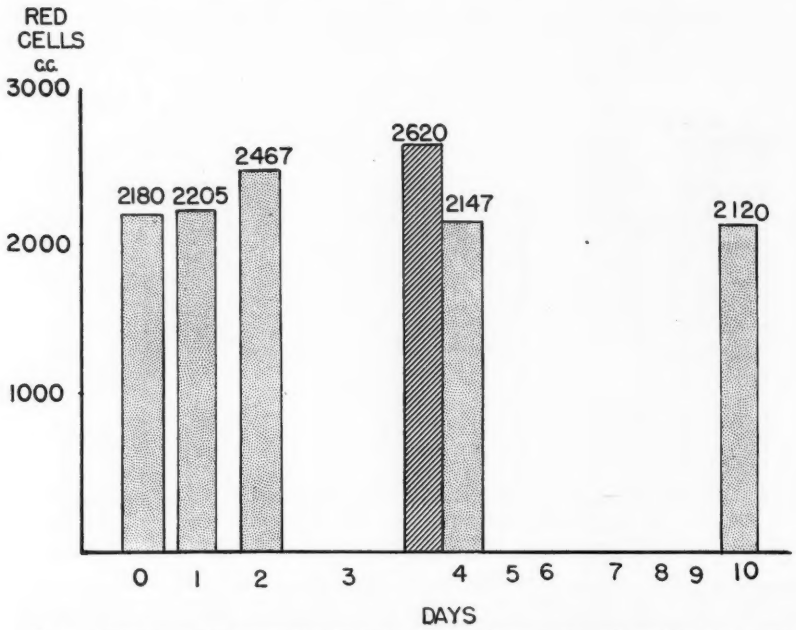

Fig. 5. Cystectomy with ureteral implantation in the colon; postoperative blood loss, 1070 cubic centimeters. The difference between theoretical and measured red cell volumes on the fourth postoperative day is 473 cubic centimeters of red cells or 1070 cubic centimeters of whole blood. Operative and postoperative loss in this case were compensated for by early and adequate transfusion (1500 cubic centimeters.)

no blood were lost other than that removed from the wound at the time of operation. The postoperative loss of whole blood is listed in the legend accompanying each figure and was computed from the difference between the theoretical red cell volume and the red cell volume actually measured by the dye method.

The first portion of this report introduced evidence to support the concept that the classical gravimetric and colorimetric methods do not measure all blood lost from the circulation at operation. It must be recognized, therefore, that a portion of the figure given as postoperative loss may represent additional operative loss not detected by the classical methods. However, as presented later, clinical evidence and autopsy findings support the statement that at least the major portion of the difference between the theoretical and actually determined red cell volume represents the previously unquantitated phenomenon of postoperative red cell loss.

Figure 4 illustrates a thoracotomy with resection of the lingular bronchus. Operative blood loss was 670 cubic centimeters of whole blood replaced with 1000 cubic centimeters by transfusion. Replacement therapy should have been more than adequate. The theoretical red cell volume of approximately 2265 cubic centimeters differs from the actual by 585 cubic centimeters of red cells or approximately 1280 cubic centimeters of whole blood. In this case the patient lost 1200 cubic centimeters of blood more than that actually measured at operation. The major portion of this was postoperative blood loss and occurred within 24 hours after the patient left the table. Clinical evidence supporting this observation was the large amount of bloody drainage postoperatively in the underwater seal drainage bottle. It is significant that even at the end of 5 weeks the red cell volume had not returned to those levels present before operation.

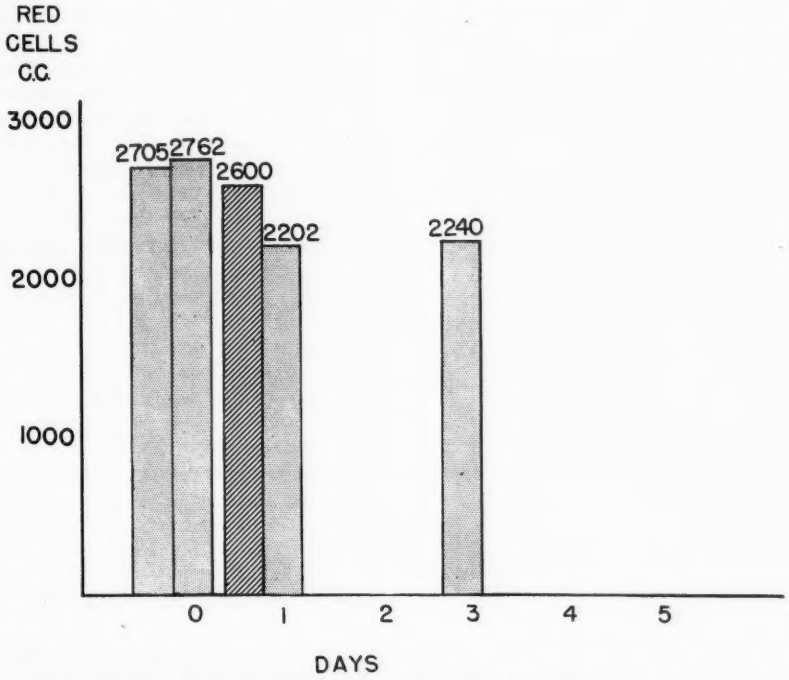

Fig. 6. Splanchnicectomy; postoperative blood loss, 865 cubic centimeters. Illustrates difference between theoretical and measured red cell volumes on first postoperative day. Difference is 398 cubic centimeters of red cells or 865 cubic centimeters of whole blood.

Figure 5 is the case of a cystectomy with ureteral implantation in the colon. The operative blood loss was 477 cubic centimeters of whole blood with replacement by 1000 cubic centimeters of whole blood at operation plus 500 cubic centimeters in the next 24 hours. The difference between the theoretical and actual red cell volumes was 473 cubic centimeters of red cells or 1070 cubic centimeters of whole blood. In this patient the postoperative loss of approximately 2 pints of whole blood occurred over a period of 4 days. The increase in red cell volume on the second postoperative day is due to transfusion therapy. The recognition and treatment of postoperative blood loss in this patient illustrates the manner in which studies of the nature described in this paper may be used to prevent uncompensated red cell loss.

Figure 6 represents a splanchnicectomy where the difference between the theoretical and actual red cell volumes was 398 cubic centimeters of red cells, a postoperative whole blood loss of approximately 865 cubic centimeters. This patient died on the seventh postoperative day of a massive coronary thrombosis. At autopsy a retropleural collection of blood estimated at 900 to 1000 cubic centimeters was observed by the pathologist. The operation was not attended by unusual blood loss, and hemostasis appeared complete at the time of closure. The major portion of the blood loss measured by the red cell volumes and found post mortem must have occurred, therefore, in the period after the patient left the operating table. According to the red cell volume determinations it occurred in the first 24 hour period. The report of Lord and Hinton offers suggestive evidence that this type of postoperative loss may be a not infrequent occurrence after lumbodorsal splanchnicectomy.

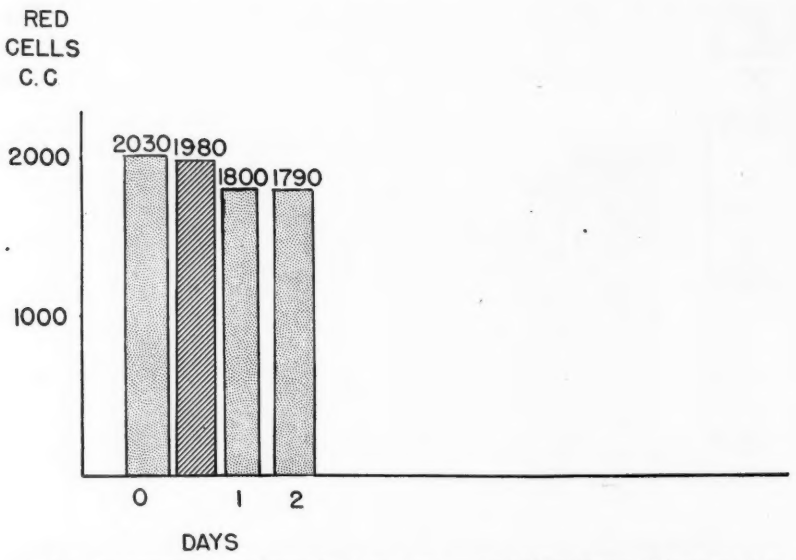

Fig. 7. Prostatectomy; postoperative blood loss, 500 cubic centimeters. Illustrates difference between theoretical and measured red cell volumes on first postoperative day. Difference is 190 cubic centimeters of red cells or in this case 500 cubic centimeters of whole blood.

Figure 7 illustrates the red cell volume changes following a transurethral prostatic resection. Operative blood loss was 110 cubic centimeters of whole blood. No transfusions were given. The difference between the theoretical and actual red cell volumes was 198 cubic centimeters which represents 500 cubic centimeters of whole blood lost over and above that measured as operative blood loss by the usual methods.

DISCUSSION

Serial red cell volume studies reported in this paper show that the operative blood loss is greater than that measured by older methods; in addition, further blood loss may occur in the postoperative period and exceed the actual operative blood loss by 100 to 200 per cent. The phenomenon of postoperative blood loss receives additional confirmation from the frequent clinical observations of the bloody drainage or thoracentesis fluid in cases undergoing intrathoracic or transthoracic procedures, the guaiac (+) stools after major gastrointestinal resections, the sanguineous drainage in the postoperative urologic case or from the perineal wound following the Miles procedure as well as autopsy findings in several cases (28). Neither excessive compensatory plasma dilution nor changes in the mean corpuscular volume of the red cell (3, 5, 24) can adequately explain the observed postoperative decreases in red cell volume or hematocrit. Increased or abnormally rapid destruction of transfused cells ordinarily does not occur (7), nor could excessive blood destruction or decreased blood formation be incriminated, for these were ruled out in this series by appropriate studies including icteric indices, bilirubin studies, and reticulocyte counts.

Due to the insidious nature of postoperative blood loss, the clinical signs customarily observed following acute blood loss may be absent. Emerson and Ebert showed that blood pressure and pulse rate need not be related necessarily to the extent of depletion of the blood volume. Similarly in this series, although postoperative blood loss amounted to as much as 1200 cubic centimeters, the concomitant alteration of blood pressure or pulse rate which might have been expected had the

loss been due to acute hemorrhage did not occur.

The available evidence suggests a parallelism between uncompensated depletions of the red cell volume and the hematocrit. Figure 8 represents changes in hematocrit observed in five patients with and without major uncompensated blood loss. Serial determinations of the hematocrit value during the preoperative and postoperative periods afford a simple laboratory test for establishing the presence of uncompensated blood loss. Although further definition of the relationship between a decreased hematocrit and the depleted red cell volume is desirable, in our experience if the hematocrit on the third postoperative day was 5 millimeters or more lower than the preoperative hematocrit, uncompensated whole blood loss in excess of 500 cubic centimeters was invariably present. It is to be emphasized that the blood sample must be drawn under standard basal conditions if the hematocrit is to be used as a simple laboratory test in establishing the presence of uncompensated blood loss. Standard basal conditions imply that the patient be fasting, flat in bed for a minimum of 1 hour, and that sampling be accomplished without prolonged venous stasis.

Severe uncompensated depletions of the red cell volume resulting from operation are replaced only over a period of weeks (12, 19, 31, 32). This is in contrast to the rapid restoration of the plasma volume and total circulating protein, which, although not restored immediately following depletion (9, 30, 36) in the adequately hydrated patient, may be restored to or above control values within 1 to 3 days (4, 19). Therefore, since plasma and cells are lost in the same proportion as they are present in the blood at operation, the hematocrit drawn immediately following surgery may be essentially unchanged from the preoperative hematocrit. However, following the restoration of plasma volume the actual red cell loss becomes fully apparent in the hematocrit decrease on the third postoperative day. Large hematocrit decreases at this time serve as a rough index of the extent of depletion of red cell volume.

Reports in the literature (16, 17, 20, 26) on the effects of massive gastrointestinal hemorrhage record changes in the electrocardiogram, the development of cardiac failure, instances of coronary thrombosis and myocardial infarction and transient or persistent amaurosis following acute blood loss. Though much further investigation is required before relating any of these complications directly to uncompensated red cell loss either as complications or sequelae, it may be significant that in specific instances where we have observed major uncompensated red cell loss we have concurrently observed (1) coronary thrombosis and myocardial infarction, (2) vague central nervous system disorders including disorientation, air hunger, and coma (3) transient amaurosis, (4) oliguria, and (5) unexplained retardation of convalescence.

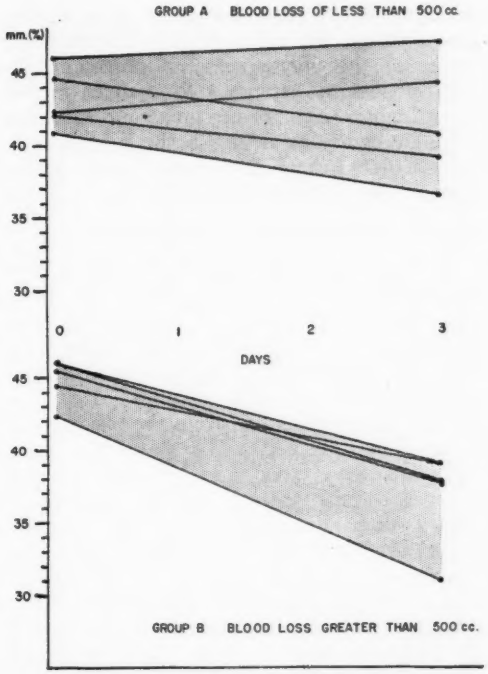

Fig. 8. Hematocrit differences observed postoperatively in compensated and uncompensated blood loss as studied by the red cell volume method. Note consistent pattern where uncompensated blood loss of 500 cubic centimeters or more is present.

Because the body unaided cannot repair rapidly severe depletions of the red cell volume the major role of blood replacement therapy

in the postoperative period is to replenish the depleted red cell volume. The surgeon aware of the phenomenon of postoperative red cell loss by attention to changes in the basal hematocrit may recognize and take the steps necessary to replenish the red cell volume depleted through uncompensated operative or postoperative blood loss.

SUMMARY AND CONCLUSIONS

1. Blood loss resulting from various surgical procedures was measured in the same patients by the standard colorimetric and gravimetric methods and compared with results obtained from repeated preoperative and postoperative red cell volumes. Red cell volumes were computed from the plasma volume (T-1824 method) and hematocrit.

2. Operative blood loss measured by the red cell volume method may be considerably higher than that obtained by the classical colorimetric or gravimetric procedures. The reasons for this discrepancy are discussed, and evidence is presented which suggests that the amount of blood removed from the wound at operation may be less than the actual amount of blood lost from the circulation at operation.

3. Observations in postoperative surgical patients are reported which suggest that postoperative blood loss may be an important complication of major surgical procedures. Even though blood lost at operation may be adequately replaced, a further insidious blood loss may occur after operation. This may be considerably larger in amount than the operative loss.

4. Extensive compensatory mechanisms operate in the human to restore a depleted plasma volume. By contrast, the ability of the body to restore a depleted red cell volume is limited. The need for recognizing and correcting a red cell volume depleted through either operative or postoperative red cell loss is emphasized.

5. It is suggested that in the adequately hydrated patient, the hematocrit value on the third postoperative day is a useful index of uncompensated red cell loss and may serve as a guide for replacement therapy.

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VAGINAL HYSTERECTOMY

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THE increasing incidence of vaginal hysterectomies performed at St. Luke's Hospital, Chicago, since 1939 warrants an evaluation of the operative procedure and the results obtained.

There is considerable variation in the attitude of gynecologists toward vaginal hysterectomy. Heaney (5, 6) has stated that vaginal hysterectomy is the operation of choice in his hands for removal of the uterus except in those cases in which it seems impossible to complete because of fixation of the uterus or because of an unusually large tumor. TeLinde (8, 9) holds that in uterine prolapse the uterus should be removed vaginally if it is diseased, either completely, or in part as in the Spaulding-Richardson operation. For uterine prolapse without uterine disease he prefers the Watkins transposition or a Manchester operation. W. C. Danforth (3) feels that vaginal removal of the uterus for prolapse is preferable to the Manchester operation.

MATERIAL

The series reported by us includes 570 vaginal hysterectomies performed at St. Luke's Hospital, Chicago, from January 1, 1939 to January 1, 1947.

PATHOLOGY

Body of the uterus. Of the 570 cases, uterine pathology was present in 295; fibromyomas were present in 234. Of these, 198 uteri were the size of a 2 to 2½ month pregnant uterus, 24 were the size of a 3 to 3½ month pregnant uterus, and 12 were the size of a 4 month pregnant uterus. Adenomyosis was encountered 33 times as the only pathologic finding and 18 times in association with fibromyomas. Endometrial polyps were found in 29 uteri and in 13 they were in association with fibromyomas. Pregnancy was present in 6 patients, carcinoma of the endometrium in 3 cases and sarcoma in a uterine fibroid was diagnosed microscopically in 3 cases.

Cervix. Early carcinoma of the cervix was encountered once. There was no gross evidence of the lesion. Small cervical polyps were present in 6 patients.

Fallopian tubes. Chronic salpingitis with adhesions was present in 3 patients.

Ovaries. Endometrial cysts were found in 6 patients. Corpora lutea, some of which were cystic and as large as 5 centimeters in diameter, were removed in 13 instances. Benign serous cystadenomas were present in 4 patients. One of the serous cysts was too large to deliver through the vagina and was removed abdominally after completion of the vaginal hysterectomy. The others were removed vaginally.

Other pelvic pathology. Endometriosis was present in 29 patients, cystourethrocele in 405 patients, rectocele in 413, and enterocele in 55. Complete uterine prolapse was present in 69 patients. Descensus of varying degree was present in 124 patients.

Normal uteri according to microscopic examination. There were 242 uteri removed that were diagnosed as normal by the pathology department. Associated pelvic pathology, as above, or altered physiology with pelvic symptoms was present in all of these patients in whom the uterus was removed. Of the 242 cases, 193 had relaxations of the anterior and posterior vaginal wall and uterine descensus. Abnormal uterine bleeding was present in 49 patients as the sole indication for removal of an otherwise normal uterus. In an additional 21 patients bleeding was in association with relaxation of the vaginal wall and descensus.

Bleeding. Abnormal uterine bleeding as the chief symptom or in association with other symptoms was present in 300 patients: 115 had menorrhagia, 27 had metrorrhagia, 110 had menometrorrhagia, and 48 had postmenopausal bleeding.

Previous surgery. Fifty-eight patients had had previous pelvic operations. Thirty-nine

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had been operated upon abdominally. Of these 15 had had uterine suspensions, 8 cesarean sections, 14 ovarian cysts removed, 1 a tubal pregnancy with removal of the affected tube and ovary, and in 1 a tumor of the uterus was removed. Thirty additional patients had had appendectomies. Five of these were associated with peritonitis and adhesions. Nineteen of the 58 patients had been operated upon vaginally, and of these, 17 had had plastic operations on the cervix or vagina, and 2 had had transposition operations.

Associated medical problems. Blood pressure of 150/90 or higher was present in 129 patients. In 12, the systolic pressure was over 200 and in 36, the diastolic was over 100 millimeters mercury. Organic heart disease was present in 29 patients. Two patients had pulmonary tuberculosis and 1 patient had bilateral chronic pyelonephritis. Five patients had a history of previous thrombophlebitis, 1 of whom had had a pulmonary embolism. Obesity was noted in 109 patients.

Operation performed. Repair of the vaginal wall in conjunction with vaginal hysterectomy was done in 450 of the 570 patients. Cystourethrocele and rectocele repair was performed upon 368 patients. Enterocele repair was done on 55 patients, 45 had rectocele repair only, and 37 had cystourethrocele repair only. The adnexa were removed in part, or *in toto*, in 23 patients. Resection of the ovary was done once. Morcellation of fibromyomas was necessary in 42 instances.

POSTOPERATIVE COMPLICATIONS

Postoperative complications occurred in 95 of the 570 cases in this series. This represents the number of lesions diagnosed. Other patients had slight elevations in temperature and in accordance with the obstetrical standard of morbidity would have to be considered morbid. The accepted standard is a temperature of 100.4 degrees Fahrenheit (oral) on any 2 days postoperatively excluding the first 24 hours. However, in these patients there were no symptoms or findings from which one could make a diagnosis of a morbid state, therefore they are not considered instances of morbidity by us. Rather, they are within the limits of the usual or average postoperative reaction observed in patients upon whom vaginal hysterectomies with repair procedures have been performed.

Patients ability to void. Of the 405 patients with anterior vaginal wall repair, 26 (7 per cent) had indwelling catheters placed in the urinary bladder. Of the 379 remaining patients, 37 (10 per cent) voided immediately and were not catheterized at all. Two hundred (53 per cent) voided during the 1st postoperative day, 129 (34 per cent) voided between the 1st and 7th postoperative day, and the remaining 13 (3 per cent) voided by the 14th postoperative day. Of the 165 patients without anterior vaginal wall repair, 5 (3 per cent) had indwelling catheters placed in the urinary bladder. Of the remaining 160 patients, 50 (32 per cent) were not catheterized at all, 101 (63 per cent) voided by the 1st postoperative day, and the remaining 9 patients (5 per cent) voided by the 5th postoperative day.

Catheterization. Of the patients with anterior vaginal wall repair, 37 (10 per cent) were not catheterized, 12 (4 per cent) were catheterized on the operative day only, 63 (17 per cent) required catheterization between the 1st and 3rd postoperative day, 93 (25 per cent) were catheterized between the 4th and 7th postoperative day, and 174 (44 per cent) required catheterization between the 8th and 23rd postoperative day. The longest period of catheterization was 23 days in a patient who developed a urinary tract infection. In the group without anterior vaginal wall repair, 50 (32 per cent) were not catheterized, 10 (6 per cent) were catheterized on the operative day only, 58 (35 per cent) were catheterized between the 1st and 3rd postoperative day, 28 (18 per cent) were catheterized between the 4th and 7th postoperative day, and 14 (9 per cent) required catheterization between the 8th and 14th postoperative day.

Indwelling catheters. Postoperative indwelling catheters are not routinely used on our service. However, in 31 patients they were indicated. In five instances the urinary bladder had been entered at the time of

operation (2 with and 3 without anterior vaginal wall repair). In the other cases an indwelling catheter was used to prevent possible trauma to the urethra from intermittent catheterization where the dissection had been extensive or where the urethral meatus was not plainly visible. The average length of time the indwelling catheter remained in the urinary bladder was 4 days, and the longest period of time was 14 days. Of the 31 patients, 8 (26 per cent) were not catheterized after removal of the indwelling catheter, 7 (23 per cent) required catheterization for 2 days only, 9 (29 per cent) required catheterization from 3 to 7 days after removal of the catheter, and 6 (22 per cent) patients required catheterization from 8 to 10 days after removal of the indwelling catheter. One patient required catheterization 16 days after removal of the catheter.

Urinary tract infection. Our criteria for the diagnosis of cystitis are: a catheterized urine specimen containing 20 milligrams of albumin or more and 10 white blood cells per high power field or more on any 2 consecutive days postoperatively. Clinical symptoms are usually present. Pyelitis is evidenced by clinical extension to the kidney region. Forty-nine patients developed urinary tract infection, 42 had cystitis and 7 had pyelitis also. Forty-one of the 49 patients had had anterior vaginal wall repair. The onset of the symptoms occurred about the 4th postoperative day on an average. The symptoms and infection subsided on an average of 8 days after onset. The average hospital stay of these patients was 16 days. The treatment used was chemotherapy, antibiotics, and general supportive measures. In this group of 49 patients, 3 had indwelling catheters in the urinary bladder. Of the remaining 46 patients, 5 (11 per cent) voided on the operative day, 11 (24 per cent) voided by the 3rd postoperative day, and 20 (43 per cent) voided by the 7th postoperative day and 10 voided between the 8th and 23rd postoperative day. All of these patients required catheterization.

Hemorrhage. Postoperative hemorrhage occurred in 9 patients. The source of bleeding was from vessels in the tissue of the vaginal vault at the operative site which had not healed by primary union. Five of these patients had had no more than the usual postoperative reaction following vaginal hysterectomy. Four of the 9 patients had a high febrile course prior to and after the hemorrhage occurred. One patient hemorrhaged on the 6th postoperative day, 2 on the 9th, 2 on the 10th, 1 on the 12th, and 1 on the 15th postoperative day. Two hemorrhaged on the 18th postoperative day requiring readmission to the hospital. Frank hemorrhage was present in 6 patients and moderate bleeding occurred in 3 patients. The vaginal vault was resutured in 5 patients; they received chemotherapy and blood transfusion. The hospital stay averaged 20 days. All of these patients recovered and at no time was their condition critical.

Shock. Moderately severe shock was present in 4 patients. This occurred at the end of difficult surgical procedures in which there was excessive blood loss during the operation. All of these patients responded to treatment for shock due to hemorrhage and their condition was stabilized within 6 to 8 hours postoperatively.

Thrombophlebitis. There was a localized phlebitis in a varicosity of the lower saphenous vein in 1 patient that occurred on the 13th postoperative day. This was treated with an ace bandage and the patient was not kept in bed. The symptoms subsided in 3 days. There was no instance of pulmonary embolism in this series.

Infection in the vaginal vault. Localized extraperitoneal infection in the submucosal tissues of the vaginal vault was positively diagnosed in 20 patients. Spontaneous drainage into the vagina occurred in all of these patients and all had a febrile course until drainage occurred. Two had large hematomas but no true pelvic abscess was noted or diagnosed. In 5 additional patients presumptive diagnosis of extraperitoneal infection in the vaginal vault was made. Drainage did not occur and the temperature elevation was slight.

Peritonitis. Generalized peritonitis occurred in 4 patients and was preceded by infection in the tissues of the vaginal vault.

The patients were discharged from the hospital on the 18th, 24th, 30th, and 42nd postoperative day.

Fistula. Two patients developed ureterovaginal fistulas. The first occurred following a vaginal hysterectomy with anterior and posterior vaginal wall repair together with a right salpingo-oophorectomy all of which was performed without difficulty. The postoperative course was uneventful and the patient was discharged on the 9th postoperative day. On the 15th postoperative day, while at home, she noticed a sudden painless discharge of fluid from the vagina. She was readmitted and an attempt to pass a ureteral catheter into the left ureter was unsuccessful. A left ureterovaginal fistula was diagnosed and a left ureterovesical transplant was performed on the 21st postoperative day. The transplant was not successful and 1 month later the left kidney was removed. The patient's recovery was uneventful and at present she is well with no apparent aftereffects. The other patient developed a fistula following a vaginal hysterectomy with anterior vaginal wall repair. During the vaginal hysterectomy there was considerable difficulty in obtaining hemostasis in the right broad ligament; the patient went into shock necessitating rapid completion of the surgical procedure. On the 4th postoperative day, she developed acute pain in the right kidney region. An attempt to pass a ureteral catheter into the right ureter was unsuccessful. A diagnosis of obstruction in the right ureter was made, due probably, to ligation of the ureter during the surgical procedure. On the 10th postoperative day, a large amount of foul fluid discharged from the vagina. She was discharged on the 21st postoperative day with a right ureterovaginal fistula to be repaired at a later time. Two months later she was readmitted with a right unilateral pyelitis. Following treatment of this, a right nephrectomy was performed. The postoperative course was uneventful and the patient is well at the present time.

Follow-up survey. Preoperative urinary symptoms were present in 338 patients. In 286 of them anterior vaginal wall repair was performed. Ninety-seven per cent (277) of the 286 patients were followed postoperatively, most of them for a period of 3 years or longer.

Recurrence of relaxation of vaginal walls. Four patients developed recurrent cystourethrocele. One patient developed a recurrent enterocele that required repair. One patient had a complete prolapse of the vaginal vault with symptoms. She was followed for 16 months, refused treatment and did not return for further management.

Recurrence of urinary symptoms. Stress incontinence was present in 163 patients preoperatively. This symptom was relieved in 156 patients following surgery. Five (3.1 per cent) continued to have incontinence after operative attempt at correction of the lesion. In 2 additional patients stress incontinence had been present since childhood and continued after the operation. Nocturia was present preoperatively in 175 and frequency was present in 186. Four (2 per cent) continued to have nocturia after surgery, and 3 (1.6 per cent) continued to have frequency after surgery.

Mortality. There was 1 death in the series. This represents an uncorrected mortality rate of 0.18 per cent. The patient, a 65 year old primipara, who was 11 years postmenopausal, was hospitalized because of complete uterine prolapse. The operation performed was vaginal hysterectomy with anterior and posterior vaginal wall repair. On the 4th postoperative day, the patient developed intermittent pain in the epigastrium associated with nausea and vomiting. The pulse rate varied between 120 and 140. The temperature remained between 100 and 101 degrees Fahrenheit. On the 7th postoperative day, the abdomen became distended, bowel sounds were absent and a generalized jaundice developed. The usual supportive measures were instituted which included Wangensteen suction, continuous oxygen and cardiac stimulants. The liver and the heart were enlarged and an auricullar fibrillation developed. The patient's condition became worse and she expired suddenly on the 9th postoperative day. The diagnosis was cardiac failure and jaundice of undetermined origin. Autopsy permission was denied.

DISCUSSION

Vaginal removal of the uterus with repair of relaxations of the vaginal walls carries with it as low a mortality rate as any of the major surgical procedures in gynecology. In our series of 570 vaginal hysterectomies, the uncorrected mortality rate was 0.18 per cent. Other clinics report similar low mortality figures. In the 2,798 vaginal hysterectomies performed by the staff of the Presbyterian Hospital of Chicago, the mortality rate was 0.21 per cent. Danforth (2) had 1 death in 600 vaginal hysterectomies or 0.16 per cent. A mortality rate of 0.66 per cent occurred in the 305 cases reported by Tyrone and Weed. In a series of 6,800 vaginal hysterectomies in the various clinics, there were 18 deaths. This represents a mortality rate of 0.26 per cent and is an enviable record for any major surgical procedure. The average mortality rate reported in more than 40,000 abdominal hysterectomies over a similar period of time and by comparable operators was 2.4 per cent. It is obvious to us that the two approaches cannot be compared accurately. We realize that many abdominal hysterectomies are of a much more difficult nature and that they could not be performed vaginally. However, when feasible, removal of the uterus through the vagina is much safer than removal through the abdomen because of the lower mortality rate.

Less often encountered causes of death are those resulting from medical complications that were present before the surgical procedure.

The death in our series was of a medical nature, precipitated by the surgical procedure, and it would no doubt have occurred whichever approach had been used. At the time of operation there was no evident medical contraindication to the surgery. The postoperative course was clearly a complication on a medical basis. We do not believe an error in judgment was involved in permitting this patient to be operated upon.

A morbidity study is not a part of this report. Gynecologic morbidity based on temperature records in accordance with obstetrical standards is not significant, is not adequate, and in no way reflects the true postoperative condition of the patient. This has been brought out in an earlier report by Jones and Doyle as it applies to abdominal hysterectomy. For this reason specific temperature reactions were not studied. Clinical evaluation of the individual patient's general condition is more pertinent in determining her postoperative status than is the presence of an elevated temperature. Temperatures to 101 degrees Fahrenheit or less during the first 3 to 4 postoperative days are quite common and are rarely indicative of a surgical complication. The temperature usually returns to normal by the 5th day.

Patients upon whom vaginal hysterectomies have been performed experience much less postoperative discomfort than do the abdominal cases. The majority of them are comfortable and require very little sedation after the first 36 hours. They have no tender abdominal incision and therefore there is no need for the abdomen to be splinted by the patient in her movements. There is much less trauma in vaginal surgery and there is no need to pack the intestines up under the diaphragm with resulting gas pains from such manipulation. A lighter plane of anesthesia is possible because of this and because relaxation of the tissues is not as necessary in vaginal surgery.

The average hospital stay in this group was 14 days. In the last year of this report it was 12.5 days. Many are able to go home in 8 days and some of them do so.

The most common complication encountered in this series was urinary tract infection. This represents 52 per cent of all complications, and it occurred in 8 per cent of all patients who had vaginal hysterectomy. Infection of the urinary bladder occurred in 41 of 49 patients who had anterior vaginal wall repair. They required repeated catheterizations and therefore were more likely to develop urinary tract infection. The group of patients that developed infection voided just as promptly as those that did not develop infection. However, they required catheterization for a much longer period of time.

Some patients, before operation, have a chronic low grade cystitis from residual urine

that accompanies a cystourethrocele. Others develop infection from repeated catheterization postoperatively. Overdistention of the bladder postoperatively may be a factor in the development of infection. Trauma to the urinary bladder that accompanies the surgical repair of a cystourethrocele may predispose to infection in the bladder. Extraperitoneal infection in the vaginal vault is frequently associated with cystitis. Vesical or ureteral fistulas are always followed by urinary tract infection. Urinary tract infection prolonged the hospital stay 2 days. Three patients had pyelitis develop 1 month after discharge from the hospital and they were readmitted for treatment. All of these patients responded to therapy and did not have disabilities at a later time.

The possibility of cutting or ligating a ureter exists by either route and may not necessarily be restricted to difficult cases. In the instance where it occurred during a difficult case, the thought that injury to the ureter might result was uppermost in the surgeon's mind during the operation. In the other it occurred during an easily accomplished vaginal hysterectomy. The possibility of ureteral injury is greater in those cases with intraligamentous fibromyomas, inflammatory masses and endometriosis. This danger also exists in complete uterine prolapse because the dissection must be extended farther out into the supporting ligaments in order adequately to perform the necessary repair of the hernia; in this way the ureter may be cut or ligated.

The incidence of fatal pulmonary embolism is less following vaginal hysterectomy than it is after abdominal hysterectomy. Erskine and Shires report that in 21,066 gynecologic procedures at Chelsea over a period of 13 years, the incidence of fatal embolism was 1 in 526 abdominal operations or 0.19 per cent. There were 13,061 vaginal procedures with an incidence of 1 fatal pulmonary embolism in 1,088 vaginal operations or 0.092 per cent. In a group of vaginal hysterectomies at various clinics in the United States, there were 3 cases of fatal pulmonary embolism in 7,000 operations. This is 1 in 2,330 or an incidence of 0.042 per cent.

The occurrence of thrombophlebitis is more frequent following abdominal hysterectomy; particularly when a patient has a history of previous thrombophlebitis, pulmonary embolism, or both. Such patients are operated upon vaginally with much more safety.

Severe shock resulting from difficult surgical procedures and excessive blood loss may occur no matter which approach is employed. The degree of shock may be minimized by anticipating its onset. The specific causes for excessive blood loss are varied. During the vaginal removal of a uterus the ligatures may occasionally slip and it may be difficult to religate the tissues; similarly the tissues may slip out of the clamp before the ligature is placed. To reduce the occurrence of these mishaps large pedicles are left on cutting the clamped tissues. Adequate hemostasis is the best safeguard against late postoperative hemorrhage.

Operative failures occurred in 10 (1.8 per cent) of the 570 vaginal hysterectomies. In 6 patients there was recurrence of lesions or relaxations as mentioned. In 8 patients there was a continuation of certain preoperative symptoms for which the patient was, in part, operated upon. It is difficult to account for the recurrences of the lesions. In some it is due to poorly developed tissues utilized for the repair. It is possible that failure to do a sufficiently extensive dissection of the enterocele might account for a recurrence of this lesion. The persistence, for 1 or 2 months postoperatively, of stress incontinence, nocturia, or frequency is not unusual. These symptoms subside where correction is obtained. Stress incontinence persisted in 5 patients for more than 3 months after surgery. In 2 patients, not counted with the above 5, stress incontinence persisted but it had been present since childhood and was not due to any lesion that could be corrected surgically. However, cystourethrocele repair was done (in conjunction with vaginal hysterectomy) in the hope that the incontinence might be alleviated, but this did not result. The 5 patients represent a 3 per cent recurrence of stress incontinence.

We have excellent results with vaginal hysterectomy and repair in the treatment of

complete and partial uterine prolapse. We feel that the main supporting structures, the uterosacral, the cardinal, and the pubocervical ligaments are more adequately utilized in the repair with the uterus removed. In most instances a prolapsed uterus occurs in women who have either had their desired number of children or who are beyond the childbearing age, and the removal of the uterus need not be questioned on this basis. Furthermore, vaginal delivery of an infant in a patient who has had a previous vaginal wall repair carries with it the likelihood of the repair breaking down. This possibility of pregnancy exists even in those patients nearing the end of their reproductive period. This is obviated with removal of the uterus at the time of the repair.

All gynecologists are familiar with the poor results frequently obtained in the medical treatment of "functional uterine bleeding." When medical treatment has been unsuccessful and surgery is necessary, hysterectomy is ideally performed by the vaginal route.

Endometriosis in its milder forms such as the subperitoneal type that does not result in adhesions may be treated by vaginal hysterectomy. However, the other forms of endometriosis that produce adhesions involving the bowel and adnexa are best handled via the abdominal approach.

Fibromyomas often can be removed through the vagina. Those of larger size are adequately managed by morcellation; this we have done with tumors as large as a 4 month pregnant uterus. The size of the tumor is not as important as is the associated fixation and position of the tumor or its integral parts. Subvesical or broad ligament tumors are best removed abdominally.

When surgery is necessary in patients with systemic medical disabilities, vaginal hysterectomy where feasible, is the safer procedure. This is particularly true in pulmonary conditions such as tuberculosis or bronchiectesis. The patients require less total anesthesia since a lighter plane of anesthesia is permissible, and postoperative excursion of the diaphragm (and lungs) is not as limited as it is in abdominal procedures. The blood pressure, blood volume, and cardiac function are not altered as much in the vaginal approach and therefore cardiac patients (organic heart disease, arteriosclerosis, hypertension) tolerate vaginal surgery with a greater margin of safety. For this reason the aged patient is more safely operated upon by the vaginal route.

Previous abdominal surgery is seldom a contraindication to vaginal hysterectomy. Appendectomies that are uncomplicated rarely interfere with vaginal surgery. However, complications such as ruptured appendices with peritonitis may cause adhesions that are very apt to increase the difficulty of vaginal hysterectomy. Previous gynecologic surgery is not often a contraindication to vaginal surgery. It is seldom that adnexal surgery makes a subsequent vaginal hysterectomy difficult and in none in this report was it a factor. Previous cesarean sections or plastic procedures on the anterior or posterior vaginal wall may produce fibrous scar tissue and it may be tedious work to find the correct plane of cleavage between the bladder and the uterus. It was in 2 such patients who had had previous cesarean sections that the urinary bladder was opened. Previous suspension operations on the uterus may result in fixation of the fundus of the uterus or the upper portion of the broad ligaments. However, the uterus can usually be brought into view with tension on the cervix and the hysterectomy completed. Those cases with marked fixation are best done abdominally. Previous transposition operations (Watkins) almost as a rule result in difficult and tedious surgery. This is not necessarily a contraindication as it would be difficult surgery if operated upon abdominally. In none of the cases in this report was it necessary to open the abdomen because of adhesions or fixation from previous surgery.

We feel that vaginal hysterectomy is superior to the Manchester operation in those cases that require repair of the vaginal walls with or without descensus. The Manchester operation is reserved for a select small group of patients who are postmenopausal and have cystourethrocele, normal well supported uteri with long cervices, and who are not good surgical risks. The operating time is shorter

(which here is important) and the results in this type of patient have been uniformly excellent.

We do not recommend the Manchester operation in younger women because some of them will require subsequent hysterectomy for uterine disease and it frequently results in difficult surgery by either route.

Ovarian tumors or cysts are best removed abdominally. The character of the tumor or cyst cannot be determined accurately before operation and it is most undesirable to rupture cysts during an operation with resultant spill of its contents into the peritoneal cavity. If an ovarian tumor or cyst is encountered during a vaginal hysterectomy, unless of small size, the hysterectomy is completed vaginally, and the abdomen is then opened to remove the cyst. There was one instance of this in our report when a serous cyst was encountered and it was removed through the abdomen after the vaginal hysterectomy had been completed.

Cancers of the uterus or adnexa should not be removed vaginally. A much wider and more adequate removal is accomplished abdominally, and in addition, a better evaluation of the extent of the malignant growth is possible. There are occasional exceptions to this policy. A very old patient with carcinoma of the endometrium is more apt to survive a vaginal removal of the uterus.

The clinical evaluation of the individual patient is usually sufficient to rule out the case with a probable carcinoma of the uterus; if not, curettage is an important aid. If question remains, the abdominal route is elected almost as a rule. In an attempt to become more familiar with the curetted endometrium and to avoid such mistakes, 2 members of the staff have routinely curetted all their patients subjected to vaginal hysterectomy since January 1, 1947. A tentative diagnosis is made at the time of the curettement.

During the 8 year period covered in this report, 27.5 per cent of the hysterectomies were performed through the vagina. During 1946, 48.2 per cent were done in this manner. This increase in the number of vaginal hysterectomies is largely due to increasing experience and this has broadened our indications for vaginal removal of the uterus.

From all of this we have established the following indications and contraindications for use in our private and ward practice, and for teaching purposes.

INDICATIONS

1. Lower mortality rate for vaginal hysterectomy and repair than for any other major gynecologic operation.
2. Lower incidence of postoperative complications.
3. Associated medical problems more safely managed when vaginal surgery is performed.
4. Better results achieved in repair of lacerations of the childbirth canal.
5. Removal of uterine fibromyomas as large as a 4 month pregnant uterus may be accomplished.
6. "Functional uterine bleeding" not responsive to medical treatment ideally treated by vaginal hysterectomy.

CONTRAINDICATIONS

1. Cancer of the uterus, tubes, and ovaries.
2. Ovarian tumors, cysts, or both, unless of small size.
3. Endometriosis unless of minimal involvement.
4. Fibromyomas that produce fixation by their position.
5. Residues of pelvic inflammatory disease.

SUMMARY

1. An analysis of 570 vaginal hysterectomies is reported.
2. A mortality rate of 0.18 per cent occurred.
3. A morbidity study is not a part of this report; more significantly, complications following vaginal hysterectomy are shown and the causes for such if determined.
4. One-half of the complications encountered were urinary tract infections and of minor nature.
5. The more serious postoperative complications, in degree of frequency were: extraperitoneal infection in the tissues of the vaginal vault, 25; postoperative hemorrhage,

9; moderately severe shock, 4; generalized peritonitis, 4; ureterovaginal fistulas, 2.

6. Better results are achieved in the treatment of relaxations of the vaginal walls and uterine descensus.

7. Previous gynecologic surgery is not often a contraindication to vaginal hysterectomy.

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EXPERIMENTAL THORACIC DUCT FISTULA

Observations on the Technique, the Absorption of Fat and Fluid from the Intestine, and Protein Depletion

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THE purpose of this paper is to describe a technique whereby a thoracic duct fistula, which will drain freely for a number of days, may be established in the dog. In addition, an attempt was made to determine how completely the lymph, drained by the thoracic duct, was excluded from the blood following the production of such a fistula. Observations were made on the absorption of fat and fluid from the intestine, and changes in the concentration of protein in lymph and serum were recorded.

THE PROBLEM

Lymph fistulas in man, following neoplastic invasion and traumatic or operative injury to the thoracic duct and larger lymph channels, are not uncommon (5, 8, 11, 15, 17, 23, 25, 26). The loss of lymph rich in protein and fat in these patients may reach enormous proportions and, if uncorrected, may have disastrous consequences. The fact that lymph fistulas develop and persist in man is in striking contrast to the difficulty encountered in the deliberate attempt to create such fistulas in animals. Until recently, efforts to produce in dogs thoracic duct fistulas, which will drain freely for more than a few hours, have been unsuccessful.

The principal difficulty encountered has been the clotting of lymph in the thoracic duct cannula. In survival experiments, the usefulness of anticoagulants is limited. Heparin applied locally in the cannula is efficient in experiments of short duration but is not practical over long periods. The prolongation of the blood coagulation is difficult to control when either heparin or dicoumarin is administered systematically to the dog. Using dicoumarin, we were unable to maintain a prothrombin level in the blood sufficiently low to prevent coagulation of the lymph in a glass cannula without endangering the life of the animal. Doses of dicoumarin of 2 milligrams per kilogram body weight daily for 3 to 6 days resulted frequently in fatal hemorrhages from the gastrointestinal tract.

A second and more successful approach to the problem of preventing coagulation of the lymph is the use of thoracic duct cannulas in which coagulation is delayed.

Zimmermann and Meyers in 1945 called attention to the delayed clotting of blood in contact with the plastic polyethylene. They demonstrated that fine tubing of this material could be used to replace the conventional intravenous needle in cases in which prolonged intravenous therapy was given.

Cain and his co-workers (6) were the first to report successful thoracic duct fistulas in dogs of 4 to 8 days' duration. These authors used small tubing of polyvinyl chloride inserted into the lower thoracic duct through a transpleural approach. In approximately one-third of their experiments they reported successful cannulations suitable for study.

In our work cannulas made from polyethylene tubing have been employed for direct cannulation of the thoracic duct in the neck. These cannulas can be made easily in a few moments over a small flame (Fig. 1).

TECHNIQUE

The technique consists of the following steps:

First, under nembutal anesthesia, the right lymphatic duct and the right cervical duct are ligated and divided, as are also all

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visible lymphatic connections between the right and left sides, and to the great veins in the mediastinum down to the pericardium. This procedure can usually be carried out without entering the pleura through a 2 inch transverse incision just above the medial portion of the right first rib. Freeman has clearly demonstrated in the dog that intestinal lymph may empty into the blood through channels other than the thoracic duct-venous junction in the neck. He found accessory connections between the thoracic duct and the right duct and between the thoracic duct and the azygos vein in the thorax. He states that such accessory connections are the rule rather than the exception. Other accessory connections are probably present in the abdomen (2). Ligature of the right duct and clearing of the superior vena cava down to the pericardium and the upper part of the azygos vein are important steps in eliminating a major group of these recognized accessory connections.

Second, 1 or 2 weeks later, after the animal has fully recovered from the first operation, the thoracic duct is cannulated under 1 per cent procaine infiltration anesthesia. The cannulation of the thoracic duct in the neck under local anesthesia, not a new (19) nor a difficult procedure, is preferable for several reasons. The general bodily changes incident to a more formidable procedure or to a general anesthesia are not encountered. Also, studies upon the ambulatory dogs can be started at once, an important consideration in an animal which is losing large amounts of fluid, fat, protein, and electrolytes through a thoracic duct fistula.

In the dog, the thoracic duct or frequently the largest branch, if there are several, empties into a lymphatic ampulla which also receives the termination of the left subclavian duct and the left cervical duct. The ampulla lies just behind the lower end of the jugular vein and empties into the blood stream by way of two ducts, one passing on either side of the jugular vein. The one passing laterally enters the blood stream at the junction of the jugular vein with the subclavian vein; the other passing medially enters the blood stream at the junction of the jugular vein with the innominate vein. The ampulla can usually be easily identified after the jugular vein is retracted laterally. The cervical duct, the left subclavian duct, and the two terminal branches of the ampulla are identified and tied off. The ampulla, with its exits to the blood thus closed, becomes distended with thoracic duct lymph. Careful dissection will reveal a distended thoracic duct coming up from below and behind the ampulla. With care being taken not to injure the duct or the immediate perilymphatic tissue, a ligature is placed, but not tied, around the thoracic duct just below the ampulla. The ampulla is then incised and the thoracic duct opening into the ampulla can be clearly seen as the lymph pours forth. A polyethylene cannula of suitable size is slipped into the opening and secured with the previously placed ligature. In this way, little damage is done to the thoracic duct distal to the cannula. Also the ampulla, fixed as it is to the surrounding tissues, makes twisting or kinking of the thoracic duct unlikely. Minor variations in the anatomical arrangement of the lymphatic terminal on the left side are common, and branches of the thoracic duct emptying either separately into the ampulla or directly into the veins should be searched for and tied. Several attempts were made to thread a polyethylene tube of small diameter distally into the thoracic duct. This was prevented after a short distance by the presence of valves which could be easily demonstrated after the duct was removed.

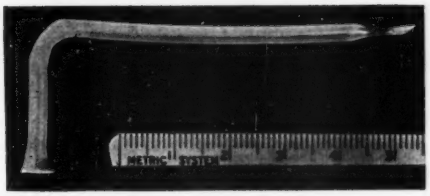

Fig. 1.

Third, the animal is placed on its feet and a plaster cast is applied from the midthorax to the angle of the jaw. A window is left for the projection of the cannula and ample openings are provided for both forelegs to allow free locomotion. The cast is an essential part of this technique. The animal can walk, sit, or lie in comfort but is prevented from moving

his neck and thus interfering with the position of the cannula. The cast should not be applied with the animal under general anesthesia, as a proper fitting for the plaster under these conditions is almost impossible.

If it is desired, 4 to 6 inches of a 12 to 18 inch segment of small polyethylene tubing can be inserted through a large needle into the right jugular vein (21) prior to the application of the plaster. The rest of the tubing is then brought out through the plaster. Into the open end of the polyethylene tube can be inserted a small needle tied onto the end of a segment of latex tubing distended with 300 to 500 cubic centimeters of fluid which is allowed to run in slowly, as suggested by Zinsser and Parkins. The distended latex tubing can be carried on a cannister strapped to the plaster on the animal's back.

Thirteen experiments using this technique have been carried out. Five were unsuccessful. The most frequent cause of failure was multiple branching of the thoracic duct at the point of termination in the neck. This cause of failure should become less, however, as experience with the technique is gained. Whereas there were 3 failures in the first 7 experiments due to this, there was only 1 failure in the last 6 from this cause or any other. The 1 other failure, also in the first 7 experiments, was due to the dog's becoming so restless that it was necessary to abandon the procedure under local anesthesia.

Six of the 8 successful cannulations drained freely from 4 to 8 days. Of the other 2, one cannula was pulled out deliberately on the third day of drainage as the contemplated studies had been completed; in the other, the cannula was accidentally removed while being cleaned on the third day of drainage. Occasionally, small clots form in the cannulas. These can be extracted usually by means of a twisting motion with a small wire in the lumen of the cannula. During the period of fistula drainage, the animals were usually docile and co-operative. In 1 experiment, however, sedative doses of pentothal sodium were required.

ACCESSORY LYMPHATICOVENOUS CONNECTIONS

To evaluate studies on an animal with a freely draining thoracic duct fistula, it is important to determine whether collateral lymphaticovenous connections are functioning.

Method. Within 1 hour of the creation of a freely draining thoracic duct fistula in 7 dogs, 2 cubic centimeters of a 1 per cent solution of the colloidal dye T-1824 were injected cephalad into a cannulated lymphatic on the dorsum of one hind foot. A second injection, into the lymphatic on the dorsum of the opposite hind foot, was carried out after the fistula had closed some time later. In all but 1, the solute for the T-1824 was the dog's own serum. In 5 experiments, the 2 injections were performed under local anesthesia. In the other 2 experiments, nembutal anesthesia was used. The appearance time of the dye was noted in the lymph flowing from the thoracic duct cannula following the first injection. Following both injections, samples of venous blood were obtained at intervals of 3 minutes to 30 minutes after the dye was injected into the lymphatic. The presence of dye in the serum was determined by either the Beckman spectrophotometer or by the Evelyn photoelectric colorimeter.

Results. The appearance time of the T-1824 in the lymph, flowing from the thoracic duct cannula after injection of the dye into a hind foot lymphatic, varied between 30 seconds and 5 minutes and 50 seconds with an average for the 7 experiments of 2 minutes and 39 seconds.

With a freely draining thoracic duct fistula, a small amount of dye was detected in the serum within 15 minutes after the dye was injected into the peripheral lymphatic in all but 1 of these control experiments. It may be of significance that in the 1 experiment in which no dye appeared in the blood, the animal was under a general anesthetic.

A lymphatic on the dorsum of the opposite hind foot was injected in an exactly similar manner after the thoracic duct fistula closed. In every case the amount of dye found in the blood serum following the closure of the thoracic duct fistula was greater than that found when the lymph was flowing unimpeded through the fistula.

It is evident that even with a freely draining thoracic duct fistula in the dog, a colloidal dye of large molecular size passes from lymphatic to blood stream somewhere between

the hind foot and the neck in the majority of animals. The amount of dye that reaches the blood in a freely draining fistula is extremely small but the blood concentration increases almost immediately if the thoracic duct is obstructed in the neck.

There is some question as to where the colloidal dye T-1824 passes from lymphatic to blood vessel. It is possible that some of the dye diffused through the blood capillary wall directly. The most likely site for this to occur would appear to be the lymph nodes. Although the colloidal dye T-1824 passes slowly from the blood stream into the tissues (13), it has not been demonstrated that this substance or the albumen to which it becomes attached passes through the capillary wall in the opposite direction. In view of the demonstration by several investigators (2, 16) of accessory lymphaticovenous connections in the dog, it seems unnecessary to postulate the diffusion of the dye through the capillary wall. The injection of a dye into a peripheral lymphatic gives no information as to possible connections between the mesenteric lymphatics and the mesenteric veins.

FAT ABSORPTION STUDY

Thoracic duct fistulas of short duration have been utilized for many years in the study of the absorption of fat from the intestine. There remains some doubt as to whether fat is absorbed solely by way of the lymphatics or whether some of it may pass directly into the portal blood. Until recently (7), general anesthesia has been employed in these studies. Also, precautions have not been taken to block the entrance of thoracic duct lymph into the blood through the right duct. The possibility that these factors may be of importance has, however, been recognized for some time (10).

Method. Fat was determined as total lipid fatty acids in the lymph and serum, according to the method of Bloor (4). Partitioning of the fatty acids was not done. In several of the earlier experiments, specimens of blood were taken for analysis from 1 to 12 hours after the administration of fat. It was found that maximum lipemia occurred usually about the fifth hour following the administration by stomach tube of 4 cubic centimeters of olive oil per kilogram of body weight. Total lipid fatty acids were determined simultaneously on the serum and lymph following the creation of the thoracic duct fistulas. The determinations were made before the administration of olive oil and on specimens taken 3 and 5 hours, and occasionally at 2 and 7 hours, after the administration of oil. In 5 healthy dogs, prefistula fat absorption studies were made approximately 1 week before the fistulas were established. Similar studies were carried out immediately following the cannulation of the thoracic duct under local anesthesia. In 3 experiments, a fat absorption study was also made on the eighth, eighteenth, and thirty-second day respectively, after the thoracic duct fistulas had closed. The animals were starved for at least 24 hours prior to each fat absorption study.

TABLE I.—FAT ABSORPTION STUDY.
TOTAL LIPID FATTY ACIDS

Experiment No.	Time hours	Prefistula serum mgm./c.c.	During fistula		Postfistula serum mgm./c.c.
			Serum mgm./c.c.	Lymph mgm./c.c.	
1	Control	4.52	3.19	2.35	
	5	5.99	3.30	72.29	
2	Control	4.28	6.42	4.03	
	5	7.35	6.24	65.30	
4	Control	3.99	4.17	5.83	4.61
	5	5.07	4.12	73.28	5.65
5	Control	4.59	3.82	2.57	5.63
	5	10.12	3.58	68.81	7.77
9	Control	3.93	4.64	3.51	4.12
	3	6.06	4.14	64.50	6.02

Results. The results of this study in 5 animals are recorded in Table I. With a freely draining thoracic duct fistula, no appreciable increase in the serum lipids is evident at the time of maximum fat absorption, as judged by the level of the total lipid fatty acids in the lymph. It is possible that small amounts of absorbed fat may have reached the blood stream, either through the portal blood or through accessory lymphaticovenous connections. Small increments in the total lipid fatty acids cannot be determined reliably by chemical methods (3). The presence of functioning

TABLE II.—EXPERIMENT 7, FAT ABSORPTION STUDY, THORACIC DUCT LYMPH

Time	Volume c.c./min.	Total lipid fatty acids mgm./c.c.
Before fluid by stomach tube Control	0.47	2.60
After 450 c.c. 5% Dextrose in 0.85% Saline by stomach tube 38 min.	0.60	8.21
56 min.	1.64	6.65

lymphaticovenous connections, other than the thoracic duct or the right duct, is evident from the fat absorption studies carried out after the thoracic duct fistulas had closed.

With sucrose or glucose as the only source of food, a definite increase in the opalescence of the thoracic duct lymph was noted following the administration of fluid by mouth up to 7 days after any fat was given by mouth. This was coincident with an increase in lymph flow. These changes were observed to occur within 10 to 30 minutes after fluid was given and continued for 2 to 3 hours. If more fluid was given after 2 to 3 hours, or after several days, this phenomenon was repeated. The increase in the opalescence was most marked in the first 30 to 60 minutes after fluid administration and became progressively less as the lymph flow continued to increase. The initial increase in the opalescence was less evident as the administration of large amounts of fluid was repeated frequently. Determination of the total lipid fatty acids in the lymph, soon after the opalescence appeared to increase grossly, revealed an increase in the fat content. The results of such a study are recorded in Table II. This dog had received no food for 72 hours prior to the creation of the thoracic duct fistula. The study was made 22 hours after the fistula was established during which time the dog received by vein about 1600 cubic centimeters of 5 per cent dextrose in water and 1600 cubic centimeters of 5 per cent dextrose in 0.85 per cent saline. No olive oil had been given. The increase in the fat content of the lymph in this dog was somewhat more marked than usual. However, no fluid had been taken by mouth for 24 hours prior to this study. The type of fluid given, whether it was water with or without glucose or saline, did not appear to make any difference in the degree of opalescence. However, as almost all of the animals were given a large amount of glucose, from which fat may have been formed (1), during the course of fistula drainage, it was not determined whether absolute starvation would elicit a greater or smaller increase in the opalescence of the lymph following fluid by mouth.

The rapid increase in the fat content of the lymph following the administration of fluid by mouth suggests that the fat lay within the lumen of the lacteals and that it was washed up by the absorption of some of the ingested fluid. It gives no clue, however, as to how the fat came to be in the intestinal lacteals or the mechanism involved in the replacement by more fat between periods of fluid administration. The experiments of Roney, Mortimer, and Ivy are interesting in this regard. They found high lipid levels in the thoracic duct lymph in dogs starved for 2 to 14 days; following enterectomy, however, no such increases were observed. They concluded that fat mobilized during starvation was transported to the intestinal mucosa where it was secreted into the intestine, the major portion being reabsorbed and passed into the lacteals.

PROTEIN STUDY

The protein concentration of the thoracic duct lymph in the dog averages 3 to 4 grams per cent (9). This is considerably higher than the concentration of protein in peripheral lymph. The difference is due to the large contribution of protein made by liver lymph (14). It is of interest to know whether there is a parallel fall of the serum protein concentration and the thoracic duct lymph protein concentration following the loss of large amounts of protein through a thoracic duct fistula.

Method. In 6 healthy dogs, protein determinations were made daily on the serum and lymph during the period of fistula drainage. A few of the early determinations were done by the copper sulfate method of Phillips and co-workers. This method was found unsatisfactory for some specimens of the thoracic duct lymph, apparently because of a lowering of the specific gravity of the lymph incident to the high fat content. The micro-Kjeldahl

method was used in all subsequent determinations. In 2 of the experiments, 4 and 8, the last protein determinations were made on the day prior to closure of the fistulas. An attempt was made to obtain specimens of blood and lymph at the same time each day, usually in the early morning before fluid administration was begun. Variations in the lymph flow between the daily samples could not be avoided. Except in experiment 2 (Fig. 3), in which a deliberate attempt was made to obtain a maximum flow of lymph, these variations were usually not great, but may have accounted for some of the irregularities in the lymph protein concentration.

Results. A progressive fall in both the serum protein concentration and the lymph protein concentration was found. The control determinations and the last determinations made while the fistulas were still draining are recorded in Table III. The loss of protein was greater than is evident from these findings, however, as in every case some degree of hemoconcentration developed. It is apparent that the loss of protein through a thoracic duct fistula in the presence of a protein free diet, in the course of a few days, will markedly reduce the serum protein concentration. Clinically, Crandall, Barker and Graham have found the loss of protein in the lymph draining from a thoracic duct fistula to be a major therapeutic consideration.

TABLE III.—PROTEIN STUDY

Experiment No.	Duration of fistula days	Serum gm./100 c.c.	Lymph gm./100 c.c.
	Control	6.46	3.41
1	4	4.18	1.87
	Change	*−2.28*	*−1.54*
	Control	5.43	3.91
2	5	3.86	0.94
	Change	*−1.57*	*−2.97*
	Control	7.08	4.35
4	5	4.22	1.92
	Change	*−2.86*	*−2.43*
	Control	*5.81	*4.10
5	8	2.71	0.34
	Change	*−3.10*	*−3.76*
	Control	6.05	3.94
7	3	3.71	1.06
	Change	*−2.34*	*−2.86*
	Control	5.83	2.30
8	3	4.14	1.09
	Change	*−1.69*	*−1.21*

*Copper sulfate method. See text.

FLUID ABSORPTION STUDY

A distinct difference in the thoracic duct lymph flow was observed in some of the earlier experiments following the prolonged administration by mouth of 5 per cent glucose in 0.6 or 0.85 per cent saline solution and 5 per cent glucose in distilled water. The ingestion of smaller amounts of these solutions did not, however, reveal appreciable differences in the volume of thoracic duct lymph flow. With a thoracic duct fistula of several days' duration, an opportunity is afforded to make observations on the variation in lymph flow following the prolonged administration of either or both of these fluids.

Method. Four experiments were performed. These were divided into two groups, with 2 experiments in each group. The first group received fluids by mouth and the second group received fluids by vein. In each experiment there were 2 periods of fluid administration. Five per cent glucose in distilled water was given in one period, and 5 per cent glucose in 0.85 per cent saline solution was given in the other. In 1 of the oral experiments, 5 per cent sucrose in 0.6 per cent saline solution was given instead. One hundred to 150 cubic centimeters of fluid per kilogram body weight were administered over a 9 to 15 hour period. The amount of fluid given, however, and the time required for administration were approximately the same for the two fluid periods in each of the experiments. When fluids were given by mouth, there was an interval of at least 2 hours between the administration of additional amounts of the same type of fluid and 8 to 10 hours between the two fluid periods. Fluids by vein were administered continuously, and there was no interval between the two fluid periods.

Results. In all of the experiments, saline solution produced a sustained and continued increase in lymph flow with a low urinary output. The prolonged administration of

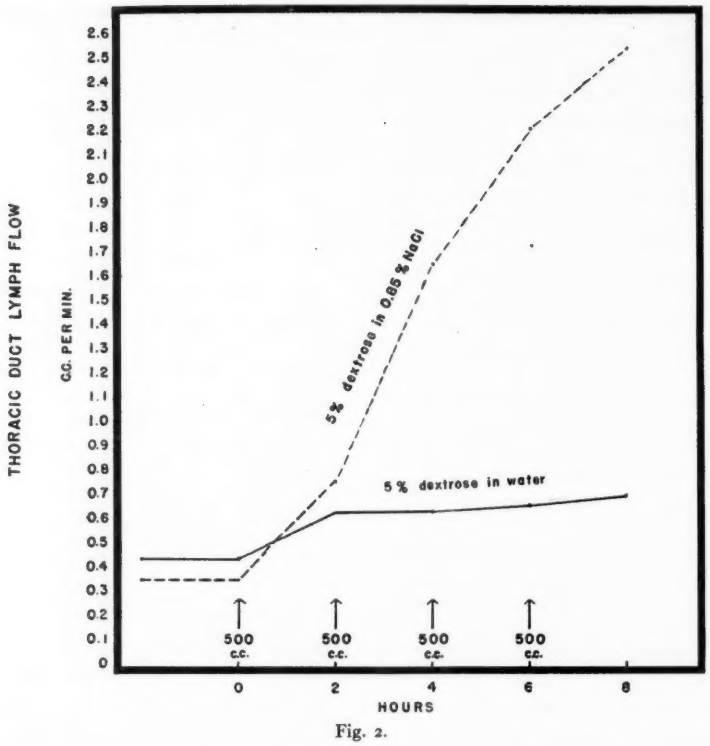

Fig. 2.

water was accompanied by a moderate initial increase in lymph flow, and a relative diuresis. In Figure 2, the thoracic duct lymph flow is recorded graphically in one of the experiments in which fluids were given by mouth. The animal was initially hypoproteinemic (not included in the normal series, Table III). Two thousand cubic centimeters of 5 per cent dextrose in water was given on the second day of fistula drainage and a like amount of 5 per cent dextrose in 0.85 per cent saline solution was given on the third day of fistula drainage. The serum protein concentration at the start of the dextrose in water was 3.15 grams per cent and on the following day at the start of dextrose in saline was 3.87 grams per cent. The values recorded are the average amounts of lymph drained per minute over successive 2 hour periods. The increase in lymph flow when saline solution was administered by mouth was much greater than when saline solution was administered by vein. In the 2 animals receiving saline solution by vein, gross peripheral edema became evident. However, edema was moderate or absent in the animals receiving saline solution by mouth. In 1 earlier experiment (Fig. 4) not included in this series, approximately 15 liters of 0.6 per cent saline, most of it with 10 per cent sucrose, was given by mouth to a 21 kilogram dog over a period of 4 days. The estimated lymph flow, based on interval collections made over a 16 to 18 hour period daily, almost equalled the fluid intake. The lymph flow stopped on the fifth day of drainage when the cannula fell out. Persistent edema in this animal was evident only at the site of the operative wounds. The estimated total amount of lymph drained, and the duration of saline administration was greater in this dog than in any other. This experiment is cited principally to show the maximum lymph flow ob-

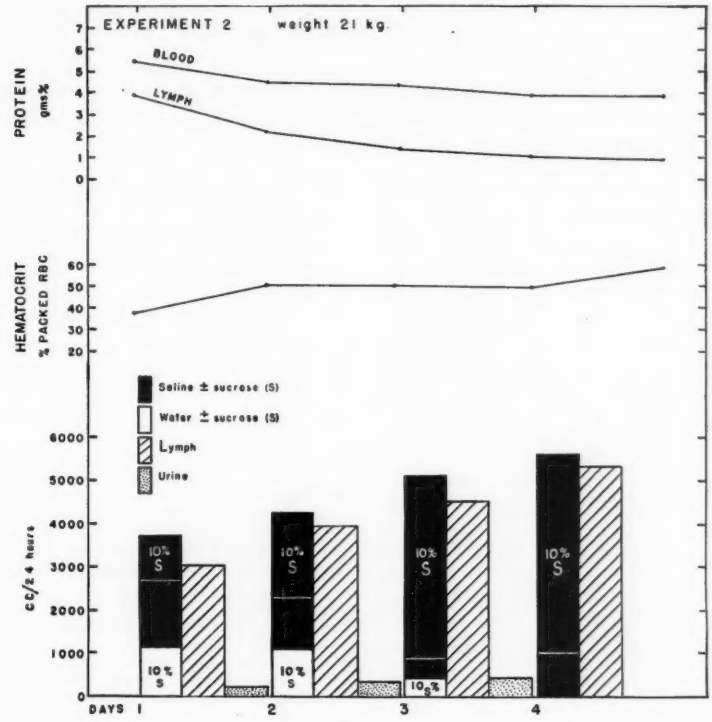

Fig. 3.

tained. It is not intended to imply that all or even a major portion of the saline solution given by mouth was absorbed into the intestinal lacteals. Other factors, such as the fact that this animal was unusually active (28), undoubtedly contributed to the maximal flow of lymph.

The difference in the thoracic duct lymph flow accompanying the administration of saline solution by mouth and water by mouth may be explained in the following manner. The moderate lymph flow that accompanied the prolonged administration of water would indicate that water was, for the most part, absorbed directly into the blood. On the other hand, relatively more of the saline solution administered in the same manner appeared to pass into the tissue spaces of the intestinal wall where it was forced into and along the adjacent lacteals by the continuous propulsive force of intestinal peristalsis. Saline solution administered intravenously accumulated in the loose subcutaneous tissue where no such involuntary propulsive muscular activity exists. One must consider the fact that during the periods of fluid administration the transudation of saline into the interstitial spaces was enhanced by the invariable fall in serum protein concentration observed in these animals (12, 24, 27).

SUMMARY

1. Thoracic duct fistulas which drained freely for a number of days have been established in 8 dogs. The thoracic duct was cannulated in the neck under local anesthesia with a cannula made from polyethylene tubing.

2. From the studies carried out with the dye T-1824, it seems probable that an abundance of accessory lymphaticovenous connections exist and that they are, as Freeman says, the rule rather than the exception. It is im-

portant, therefore, that in the interpretation of experimental data with a thoracic duct fistula, one considers the possible functional significance of these accessory connections.

3. In the presence of a thoracic duct fistula, the administration of olive oil by stomach tube did not cause an appreciable rise in the total lipid fatty acids in the serum at the time of maximum fat absorption as judged by the lipid content of the thoracic duct lymph. This does not mean, however, that fat may not have reached the blood through direct portal vein absorption or through accessory lymphaticovenous connections. It only indicates that in the presence of an unobstructed thoracic duct, the absorption of fats by any other route must be small.

There was an increase in the lipid content of thoracic duct lymph following the administration of fluids by mouth to dogs whose only source of food was glucose or sucrose. The experiments suggested that fat was being continuously replaced in the intestinal lacteals. The mechanism of this replacement was not determined.

4. There was a progressive loss of protein through the thoracic duct fistula. This resulted in a rapid fall in the protein concentration of both lymph and blood. In general, the fall in serum protein concentration paralleled the fall in lymph protein concentration.

5. Glucose in saline solution by mouth resulted in a greater increase in thoracic duct lymph flow than did glucose in water by mouth, or glucose in saline solution or water by vein. Some of the factors of importance in the interpretation of these observations are: the propulsive force of intestinal peristalsis; depletion of serum proteins; different rates of excretion of these fluids by the kidneys.

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EWING'S TUMOR

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THE purpose of this article is primarily to report the apparent cures of 3 patients with Ewing's tumor of bone (in one of whom there was disappearance, without direct treatment, of an apparent pulmonary metastasis), and secondarily to summarize the features of all cases of Ewing's tumor which have been seen at the Vanderbilt University Hospital since 1925.

INCIDENCE

General. Since 1925 there have been 192 specimens of bone tumors, exclusive of metastases, submitted to the Surgical Pathology Laboratory, of which 71 were malignant. The 20 Ewing's tumors found in this series thus represent an incidence of 10 per cent of all bone tumors and 28 per cent of malignant bone tumors.

Race. Geschickter and Copeland (35) noted the occurrence of Ewing's tumor in only 1 negro in a total of 122 patients with such tumors, whereas 2 of our 20 patients were negroes.

Sex. Like other observers (35), we found that Ewing's tumors are more frequent in males, there having been 13 males and 7 females.

Age. The youngest patient was 3 and the eldest 43 years of age. There were 5 patients in the first decade, 9 in the second, 3 in the third, 1 in the fourth, and 2 in the fifth. The occurrence of Ewing's tumors in patients over 40 years of age is unusual, but Geschickter and Copeland (35) reported 2 such cases in patients 44 years of age, and Stout (87) stated that "the age variation extends from 4 to 79 years." Eighty per cent of our patients were less than 25 years of age.

Site. (Table I). In contradistinction to the findings of Ewing (32) and Geschickter and Copeland (35), but like Stout (87) and Lichtenstein and Jaffe (61) we found the tumors more frequently in flat bones (14 cases) than in long bones (6 cases). Five of the tumors of the long bones originated in the diaphysis, only 1 of these 5 having arisen in the region of the metaphysis. In the sixth patient the roentgenogram of the femur showed involvement of both the metaphysis and the epiphysis so that it was impossible to state the exact site of origin of the tumor.

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SUBJECTIVE MANIFESTATIONS

Duration of symptoms. The periods which had elapsed from the onset of symptoms until the application to this clinic for treatment ranged from 5 weeks to 12 months, the average time having been 5 months for all patients and slightly less than 5 months for the individuals who died. The patients still alive had had symptoms for 4, 4, and 10 months, respectively.

Injury. The question as to whether injury may be a factor in causing a bone tumor or whether it simply calls attention to an area in which the lesion is already present has never been settled. However, in instances in which a tumor occurs at a site which, a few weeks before, was subjected to a severe blow one hesitates to deny the possibility of such trauma as an etiologic agent. In 10 patients there was no injury, while in each of the other 10 there was a definite history of a severe injury; however in 1 patient injury occurred 25 years before admission. In 1 instance, the interval between injury and swelling was not recorded and in another it was stated to have been "several weeks." In 2 individuals pain occurred at the time of the injury and did not subside, the swelling having been noted 3 days later in 1 patient (Case 2) and 2 months later in the other. In the 5 remaining patients the injury preceded the occurrence of pain or swelling by intervals of 1 week, 1 month, 2 months, 10 months, and 10 months.

Fig. 1. The roentgenogram of the scapula shows new bone formation in the so-called "sunray" fashion which is often considered highly suggestive of osteogenic sarcoma. Microscopic section of the tissue removed at exploration showed Ewing's tumor.

Pain. The occurrence of pain was recorded in all instances except that of a child with a tumor of the scapula, who was brought to the hospital because his parents noted the presence of a mass.

Swelling. Swelling was noted by the patient or his family in all instances except 1 in which the tumor was in the twelfth rib. In 10 patients there had been a slow increase in size, in 4 the increase had been rapid, in 1 patient there had been no change since the mass was first noticed (9 weeks before admission to the hospital), and in 1 patient the presence or absence of this symptom was not recorded. There was a definite history of fluctuation in the size of the tumor in each of 3 individuals. One patient developed a swelling which subsided completely and then recurred and persisted until time of admission to this clinic. In 2 patients the swelling occurred, subsided completely, recurred and subsided, and again recurred and subsided before the third recurrence which failed to regress before treatment.

TABLE I.—SITE OF EWING'S TUMOR

Author	Flat bones	Long bones
Ewing	4	6
Geschickter and Copeland	48	78
Lichtenstein and Jaffe	12	5
Stout	24	18
Present series	14	6
	Rib 4 Ilium 2 Ischium 2 Sacrum 2 Scapula 2 Mandible 1 Clavicle 1 14	Femur 3 Fibula 2 Tibia 1 6

Fracture. A spontaneous fracture occurred in only 1 instance, the patient having fractured the shaft of the femur 15 months after injury and 5 months after the appearance of the tumor.

PHYSICAL AND LABORATORY FINDINGS

Evidence of inflammatory disease. There was some evidence of inflammatory disease in all patients. Every individual had an elevation of temperature before operation to 99 degrees F. or more. In each of 14 patients there was a rise in temperature before operation to 100 degrees or more, the maximum temperature in any patient having been 103 degrees. In 15 patients there was tenderness over the involved area. In 9 instances it was noted that the skin over the tumor was warmer than it was elsewhere, in 1 instance there was a statement that the skin was not warmer, and in 10 patients the presence or absence of this sign was not recorded. The minimum leucocyte count was 5,200 and the maximum was 18,000. In 10 patients the white blood cell count was 10,000 or more. The evidence of inflammatory disease was so striking that, before admission, aspiration had been done in 1 instance and incision and drainage in another and, in this clinic, incision and drainage were done in 1 patient.

Characteristics of the tumor. In most instances, the tumors were visible and in all patients they were palpable. Most of the tumors were smooth and all of them were firm or hard, and immovable. Although none was fixed to the skin, one (a tumor of the mandi-

TABLE II.—PREOPERATIVE DIAGNOSIS

	Clinical	Roentgenologic
Flat bones		
Ewing's tumor	4	5
Tumor	7	3
Tumor or inflammation	0	2
Inflammation	2	1
Cyst	1	1
Long bones		
Ewing's tumor	2	0
Sarcoma	3	4
Osteomyelitis	1	2
Total	20	18[1]

[1]One patient with a tumor of the scapula did not have a preoperative roentgenogram because the diagnosis was thought to be acute osteomyelitis. Another patient with a tumor of the twelfth rib had a preoperative roentgenogram elsewhere before admission to the Vanderbilt University Hospital. Therefore there is a discrepancy in the totals.

ble) was ulcerated, having been incised before admission.

Erythrocyte count. In 4 patients the erythrocyte count was below 4 million and in 7 it was below 4.5 million. The range in the other individuals was from 4.5 to 5.5 million. The minimum count was 2.7 million, the maximum 5.5 million.

ROENTGENOLOGIC FINDINGS

The roentgenologic findings (Table II) in our patients were so variable that the diagnosis of Ewing's tumor was made by the roentgenologist in only 5 of the cases which occurred in the flat bones and in none of those which occurred in the long bones. In the patients with tumors of the flat bones the changes were thought to be due to tumor or inflammation in 2 instances and to inflammation in 1 instance. The changes in 2 of the tumors of long bones were thought to be due to osteomyelitis. In 1 instance the so called "sunray" picture (Fig. 1) was seen and in another patient the characteristic roentgenologic findings of a bone cyst (Figs. 2 and 3) in the twelfth rib were observed. In 1 instance in this clinic the fairly characteristic "onionpeel" appearance has been seen in a bone lesion which on microscopic examination proved to be an osteogenic sarcoma. However, since the occurrence of this onionpeel formation is quite unusual in any bone disease other than Ewing's tumor, we believe that such a finding is highly suggestive but not pathognomonic of Ewing's tumor.

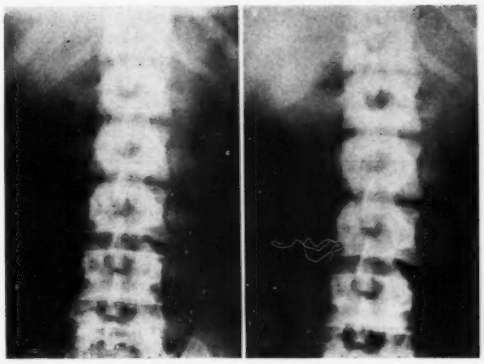

Fig. 2, left. This roentgenogram, a plain film of the abdomen of a patient thought to have acute appendicitis, shows a lesion of the twelfth rib which the roentgenologist believed to be a bone cyst.

Fig. 3. The roentgenogram of the same patient whose film is shown in Figure 2. Even after a period of 11 months the roentgenologic findings resemble bone cyst more than Ewing's tumor. The rib was excised and microscopic sections showed Ewing's tumor.

OPERATIVE FINDINGS AND GROSS PATHOLOGICAL CHANGES

Exploration in some instances revealed a false capsule which was probably periosteum, but in most of the patients there was invasion of the muscle by tumor. Some of the tumors were not very vascular but a few showed extreme vascularity, one of them necessitating the insertion of a gauze pack to control the bleeding which followed excision of tissue for microscopic examination. The color of the neoplastic tissue was gray in the majority of the patients, but in some it was red or purple, because of hemorrhage. Some of the tumors were firm and others were soft and friable.

MICROSCOPIC FINDINGS

There was no stroma between the individual cells, but in most instances there were coarse strands of connective tissue which divided the cells into groups (Figs. 5, 9, 15, and 21). Erythrocytes were present in most of the sections. Striated muscle had been invaded by tumor in several instances. Perivascular or perithelial arrangement of cells was noted in the sec-

TABLE III.—TREATMENT AND RESULTS

Treatment	Bones involved		Total No. of patients	Average survival time of patients who died (mos.)	No. of patients living and well
	Bone	No. of bones			
Irradiation only	Pelvis	6	14	12.5	1
	Rib	2			
	Scapula	2			
	Femur	2			
	Clavicle	1			
	Tibia	1			
Excision and irradiation	Rib	2	2	43	0
Biopsy, irradiation, and amputation	Fibula	1	1		1
Amputation	Femur Fibula	1 1	2	9	1
No treatment	Mandible	1	1	1	0

tions from only 4 patients. Although all of the sections of all of the patients were repeatedly studied only one formation in one section was seen which resembled the rosette seen in neuroblastoma. The nuclei of the cells were round or oval. The chromatin in most cases was finely divided but in a few it was fairly coarse. In 5 instances a single central nucleolus was seen in a type of cell in which the chromatin was fairly coarse. In the majority of sections the cells showed practically no cytoplasm, and in the cells in which cytoplasm was visible it was small in amount and slightly acidophilic in staining reaction. The cell border was indistinct except in one section. There was usually very little variation in the size of the cells. Mitotic figures were few in all except 2 instances, in which they were fairly frequent, being as many as 4 per high power field in one and 3 per high power field in the other. The microscopic pathologic changes were fairly constant and were considered to be typical in 12 of the tumors. In the 8 other tumors, the microscopic findings, although not perfectly typical, were characteristic enough to make the diagnosis of Ewing's tumor incontrovertible.[1]

TABLE IV.—DURATION OF LIFE IN FATAL CASES

Patients	Months
5	0 to 6
5	7 to 12
4	13 to 24
1	27
1	54
1	59
Minimum	1
Maximum	59
Average	15

DIAGNOSIS, TREATMENT, AND RESULTS

We believe that it is impossible to make an unequivocal diagnosis of Ewing's tumor by means of the roentgenogram alone and that all such lesions should be subjected to exploration and removal of tissue for microscopic examination. Furthermore, it seems unwise to administer roentgen ray therapy as preoperative therapy or a so called therapeutic test without microscopic confirmation of the diagnosis. Tissue examined after roentgen ray therapy sometimes does not show pathologic changes definite enough to justify the diagnosis of Ewing's tumor and thus the true nature of the disease must always remain open to question. In one case in point (Case 2) the fibula was explored and tissue was removed which showed Ewing's tumor (Fig. 9). Inasmuch as the parents of the patient would not permit her to be subjected to an amputation, roentgen ray therapy was given. Later, consent having been obtained, amputation was done, and, although sections were cut from 5 different sites, a definite diagnosis of Ewing's tumor could not be made (Fig. 11). In instances of probable Ewing's tumor in a bone such as the ilium, which cannot be removed without extreme mutilation of the patient, tissue for microscopic examination should be removed before roentgen ray treatment is started. In short, the diagnosis of Ewing's tumor should be made by microscopic examination before amputation is done or roentgen ray therapy is administered. In a case of probable Ewing's tumor in a rib, excision of the rib may be done without previous biopsy.

[1]Microscopic sections of the tumors herein reported in detail (Cases 1 to 4) were reviewed by E. W. Goodpasture, professor of pathology at Vanderbilt University Medical School, and N. C. Foot, professor of surgical pathology at Cornell University Medical College. Dr. Goodpasture agreed with our diagnosis in all instances. Dr. Foot thought that the diagnoses in Cases 1, 2, and 4 were Ewing's tumor. In regard to Case 3 Dr. Foot stated that it "could be Ewing's tumor. The invaded muscle looks like it but the bone-marrow has the appearance of harboring a growth that is more like angiosarcoma with perithelial proliferation. That type of tumor is one of Ewing's 'endotheliomas of bone."

Fourteen patients were subjected only to biopsy and irradiation. One tumor was in the tibia and the patient should have been subjected to amputation. It was shown by Lichtenstein and Jaffe (61) that inspection of the gross specimen of a long bone may reveal that the tumor has spread farther than one is led to believe by the roentgenogram. This observation justifies the statement that amputation should be done not through the involved bone but through the bone proximal to it. Thus amputation should be done through the femur for Ewing's tumor of the tibia. In instances of Ewing's tumor of the femur we believe that hip-joint disarticulation should be done, but of our 3 patients with Ewing's tumors in the femora, 2 were subjected only to biopsy and irradiation and the third to high thigh amputation. In cases of Ewing's tumor of the shoulder and pelvic girdle the question of whether to advise radical surgery or irradiation is not definitely settled. Such operative procedures as shoulder girdle amputation and hemipelvectomy are extremely mutilating and are especially undesirable in the young patients affected by this disease. The other two factors which make this subject a controversial one are that cures even by such radical procedures are extremely rare, and that a few patients are cured by roentgen ray therapy alone. We believe that amputation through the humerus or femur and not simple excision of the involved bone should be done for Ewing's tumor of the radius or fibula because of the fact that the greater possibility of cure by amputation outweighs the advantage of the better functional result by simple excision.

Table III shows the sites of involvement, the treatment, and the duration of life after the diagnosis had been made. Of the 14 patients subjected only to biopsy and irradiation, there is only 1 who is still living. Both patients on whom excision of the ribs was done and followed by irradiation are dead. One patient subjected to biopsy, irradiation, and amputation is alive. One of the 2 patients subjected to amputation alone is alive. One patient in whom no treatment was given is dead. Table IV shows the duration of life, after the establishment of the diagnosis, of our 17 patients who died. Five patients survived less than 6 months and 10 patients survived less than 12 months.

Meyerding (69) from the Mayo Clinic reported that of 114 patients, in 100 of whom the diagnosis had been confirmed by microscopic examination, 21 lived 5 or more years (18.4 per cent). Geschickter and Copeland (35) reported 5 year cures in 6 of 99 patients (6 per cent) who were followed. Coley (13) stated that 3 of 70 patients (4.3 per cent) followed were alive and well 5 or more years after the diagnosis had been established. None of Lichtenstein and Jaffe's (61) 17 patients lived 5 years. Including the 20 patients herein discussed, 3 of whom survived 5 or more years (15 per cent), the total number is 320, with 5 year survivals in 33, or approximately 10 per cent. In a review of the literature on Ewing's tumor it was found impossible to determine accurately the total number of such cases reported and the total number of 5 year cures because some workers reported 5 year survivals without mentioning the total number of tumors they had seen, others reported cases without mentioning 5 year survivals, and still others reported cases which had been reported previously. However, it is thought worth while to report our observations from the literature. The reports were divided into 3 groups: (1) those in which the author gave the total number of cases and the number of 5 year survivals (Table V); (2) those in which 5 year survivals were reported without mention of the total number of cases seen (Table VI); and (3) cases reported without mention of 5 year survivals (Table VII). In group 1 were 386 patients with 48 five year survivals; in group 2 were 3 patients with 3 five year survivals, and in group 3, 176 patients, survivals not mentioned. A summary of the findings in these tables shows that of a total of 565 cases of Ewing's tumor reported in the literature, 51 patients, or 9 per cent, survived 5 years. Nowhere in the literature was a report found in which it was stated that the metastasis from a Ewing's tumor disappeared, without treatment of the metastasis.

CAUSE OF DEATH

Although none of the patients died in the hospital, the reports from the families, family

TABLE V.—REPORTS FROM LITERATURE OF NUMBER OF PATIENTS AND NUMBER OF 5 YEAR SURVIVALS (GROUP 1)

Author	Total No. of patients	No. of 5 year survivals
Bergstrand (3)	4	1
Brunner (5)	5	1
Campbell (7, 8)	30	7
Clopton (12)	5	1
Coley (13)	70	3
Geschickter (35)	99	6
Hamilton (43)[1]	21	3
McGuire (66)[2]	2	1
Meland (67)	7	2
Meyerding (69)	114	21
Potozky (79)	4	1
Swenson (88)	25	1
Total	386	48, 12.4%

[1]Hamilton (43) reported 37 patients but 16 of them were included in the article by Campbell (7).

Other articles reviewed but not included in above table:

Christensen (10)—Patients reported in this article were reported later by Crowell (26).

Coley (14–21)—The patients in these articles are included in that of Coley (13).

Connor (22) reported 54 patients with two 5 year survivals but a later article (23) stated that not all of them were cases of Ewing's tumor. Therefore these patients are not included.

Crowell (26) reported 105 patients with nine 5 year survivals. These patients were all of those from the Bone Sarcoma Registry through 1935, the majority of which have been reported by other authors. If they were included, the figures above would be changed to 491 and 57.

Desjardins (28–29)—The patients reported in these articles were included in the one by Meyerding (69).

Ewing (31–32)—The patients reported in these articles are included in the paper of Coley (13).

Geschickter and Maseritz (36)—These patients were included in Reference (35).

[2]This five year survival was also reported by Smith (85).

doctors, and the Bureau of Vital Statistics led us to believe that the deaths of all 17 patients were due to the effects of the tumors. On the roentgenograms there were demonstrated metastases to the lungs in 8 patients, 2 of whom also had metastases to the skull. In 1 individual, skull metastases without pulmonary metastases were seen. In 1 of the patients with metastases to the lungs and skull, there were metastases to the pelvic bones.

TABLE VI.—FIVE YEAR SURVIVALS, IN THE REPORTS NOT GIVING THE TOTAL NUMBER OF PATIENTS SEEN BY THE AUTHORS (GROUP 2)

Author	No. of five year survivals
Nielsen (72)	2
Wilson (94)	1
Total	3

TABLE VII.—PATIENTS REPORTED WITHOUT 5 YEAR SURVIVALS (GROUP 3)

Author	No. of cases	Author	No. of cases	Author	No. of cases
Ahlstrom (1)	2	Hankey (44)	1	Oberling (73)	12
Barden (2)	1	Hellner (45)	6	Oppikofer (74)	2
Brav (4)	1	Herbert (46)	2	Papadopoulos (75)	1
Brunschwig (6)	3	Imler (47)	1	Pfahler (76)	1
Cabot (62, 63, 64)	3	Ishihara (48)	1	Pomeranz (77, 78)	4
Carrell (9)	6	Keatinge (49)	1	Pritchard (80)	1
Clegg (11)	1	Kirklin (50)	6	Reuben (81)	2
Connor (23)	3	Klein (51)	1	Roberts (82)	1
Craver (24)	1	Knutsson (52)	1	Sevier (83)	1
Crockett (25)	1	Koster (55)	1	Sloat (84)	1
De Santo (27)	1	Lattman (56)	3	Stewart-Harrison (86)	8
Dupont (30)	1	Lee (57)	1	Swenson (89)	1
Foote (33)	1	Leotta (58)	1	Sycamore (90)	1
Forbes (34)	1	Leri (59)	1	Tavernier (91)	1
Gharpure (37)	1	Leriche (60)	1	Troell (92)	4
Goyle (38)	1	Lichtenstein (61)	17	Williams (93)	1
Gratz (39)	1	Mathieu (65)	1	Zimmermann (95)	1
Gunsett (40)	1	Meyer (68)	1	Zuppinger (96)	1
Haberler (41)	4	Morton (70)	1	Total	134
Hall (42)	3	Neely (71)	5		

Other articles reviewed but not included in above table:

Kolodny (53, 54). The patients reported in these articles are included in the report by Crowell (26).

Stout (87) discussed Ewing's tumor but presented no cases.

Geschickter and Copeland (35), reporting 122[1] cases of Ewing's tumor stated, "Enlargement of the lymph nodes was reported in 16 cases, and in 8 was proved by microscopic examination." No evidence of metastases to the lymph nodes was noted in any of our patients.

CASE REPORTS

CASE 1. Surg. Path. No. 2955, Registry of Bone Sarcoma No. 2305.

The patient was a white girl 11 years of age who was admitted to the Vanderbilt University Hospital on December 16, 1930, complaining of a swelling of the left leg of 10 months' duration. One year previously, she fell on a log, striking the lateral aspect of the leg just below the knee. Two months later she noticed a slight swelling of the leg. Three weeks before admission to the hospital she had fever and noted redness, tenderness, and increased warmth of

[1]Although Geschickter and Copeland reported 122 cases of Ewing's tumor only 99 of these patients were included in their follow-up study.

Fig. 4a.

Fig. 4b.

Fig. 6.

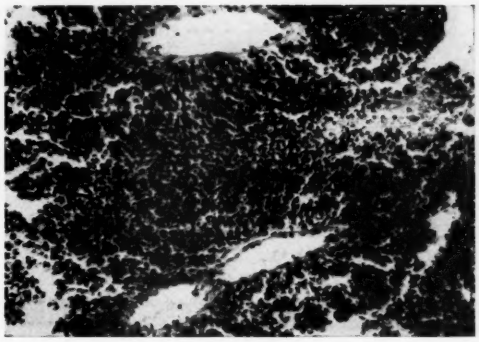

Fig. 5.

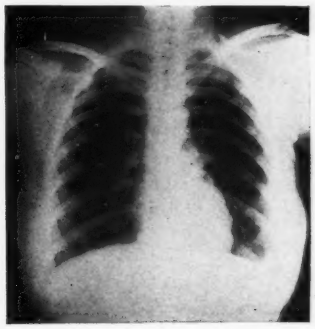

Fig. 7.

Fig. 4. Case 1. The roentgenogram shows, in the fibula, both "onionpeel" and "sunray" formations, that is, there is new bone formation both parallel and perpendicular to the shaft of the fibula.

Fig. 5. Case 1. The photomicrograph shows Ewing's tumor cells in the perithelial or perivascular formation.

Fig. 6. Case 1. The roentgenogram of the stump of the femur made more than 17 years after amputation shows no evidence of neoplastic disease.

Fig. 7. Case 1. No evidence of metastasis is present in the roentgenogram made more than 17 years after the establishment of diagnosis of Ewing's tumor of fibula.

the leg. Aspiration by her family physician obtained blood.

At the time of admission to the hospital, the patient's temperature was 99 degrees F. and it rose to 100 degrees F. the next day. On the lateral and posterior aspects of the leg there was a firm slightly tender, poorly circumscribed mass. Over the tumor the veins were prominent and the skin was warmer than elsewhere. The leucocyte count was 9,600.

The roentgenogram (Fig. 4) showed a soft tissue tumor of the upper portion of the leg, destruction of the upper end of the shaft of the fibula, and new bone formation both parallel and perpendicular to the shaft of the bone. The film of the chest showed nothing abnormal.

The clinical and preoperative roentgenologic diagnosis was osteogenic sarcoma.

A tourniquet was placed 1 inch above the femoral condyles and an incision was made over the tumor. After the thinned cortex had been opened, soft tumor tissue was seen, frozen section of which showed malignant tumor. A second tourniquet was placed high on the thigh and a midthigh amputation was done between the tourniquets.

On microscopic examination (Fig. 5) the cells were found to be quite uniform with a very small amount

of cytoplasm and indistinct cell borders. The nuclei were round or oval and basophilic, and contained chromatin which was fairly finely divided. The perivascular or perithelial formation was quite marked. Although there was very little stroma, a few septa of connective tissue could be seen. The tumor cells had extended into the striated muscle.

Roentgen ray therapy was not given. On April 16, 1948, more than 17 years after operation, her general condition was found to be excellent. The patient was able to walk very well with the help of the artificial extremity. The stump was normal. There were no palpable masses in the stump, inguinal region, or abdomen. Roentgenograms of the stump (Fig. 6) and chest (Fig. 7) showed no evidence of recurrence or metastasis.

The biopsy was done distal to a tourniquet proximal to which amputation was done. Such a procedure, when possible, seems advisable, to prevent dissemination of the tumor during exploration. However, Case 2 reveals the fact that this procedure is not always necessary to effect a cure.

CASE 2. Surg. Path. No. 10153, Registry of Bone Sarcoma No. 2297.

The patient was a white girl 16 years of age who was admitted to the Vanderbilt University Hospital on July 1, 1938, complaining of a swelling of the left leg. Four months before admission to the hospital she fell from a truck and injured the lateral part of the left leg. Three days later, swelling, bluish discoloration, and pain occurred. After a few days these signs subsided to some extent, but they again began to increase 2 months later.

On the day of admission to the hospital, her temperature was 99 degrees F. At the junction of the middle and lower thirds of the left leg, there was an annular, firm, slightly tender swelling. The skin over the tumor showed redness and increased warmth. The leucocyte count was 12,000.

Just distal to the middle of the shaft of the left fibula, there was an irregular area of destruction (Fig. 8). The roentgenogram of the chest showed nothing abnormal.

Although the roentgenologic diagnosis was osteomyelitis, the clinical diagnosis was malignant tumor, probably Ewing's tumor.

A posterolateral incision was made over the site of maximum swelling. The fibula was rough and surrounded by gray, soft, friable tissue which had extended into the muscle. Several pieces of fibula and tumor were removed and the wound was closed with silk.

On microscopic examination the cells were found to be fairly uniform with very little cytoplasm (Fig. 9). The nuclei were round or oval and basophilic. In the majority of the nuclei the chromatin was finely divided but, rarely, a central nucleolus was present. There were a few areas of necrosis. Tumor cells were seen in bone and in striated muscle.

The parents of the child were told that amputation should be done but they refused to give their consent. Seven days after the biopsy the wound disrupted. Twenty-three days after the biopsy roentgen ray therapy was begun and over a period of 14 days a total of 1,000 roentgens was administered to each of 2 portals over the leg (Fig. 10) and 1,200 roentgens to the left inguinal region. At this time the parents gave permission for an amputation. Forty-three days after biopsy a supracondylar femoral amputation was done.

On microscopic examination, although sections were made from 5 sites, a definite diagnosis of tumor could not be made (Fig. 11). There were a few areas in which cells with round nuclei and little cytoplasm could be seen, but these cells resembled lymphocytes more than cells of Ewing's tumor. There had been considerable replacement of striated muscle by connective tissue.

This patient was delivered of a normal infant July 8, 1947. On February 21, 1948, more than 9 years after amputation, she was in excellent health. She was able to walk very well, using the artificial limb. Examination revealed a well healed incision with a smooth bone end and no inguinal or abdominal masses. A roentgenogram of the stump (Fig. 12) showed no recurrence and a roentgenogram of the chest (Fig. 13) showed no metastases.

Inasmuch as 43 days elapsed between the biopsy and amputation, what would appear to be adequate opportunity for dissemination of the tumor was present. The roentgen ray therapy was administered because permission for amputation could not be obtained. We see no reason for irradiation preceding amputation.

CASE 3. Surg. Path. No. 13468. Not registered with the Registry of Bone Sarcoma.

The patient was a white girl 17 years of age who was admitted to the Vanderbilt University Hospital on December 26, 1940, complaining of pain in the right hip. There had been no injury. Four months before admission to the hospital she began to have pain in the hip and 2 months later she noticed that the right hip was larger than the left one.

The temperature was 99.2 degrees F. In the medial portion of the ilium there was a firm, nontender, poorly circumscribed mass over which the skin was warmer than elsewhere. The leucocyte count was 7,200.

A roentgenogram showed an area of destruction in the medial portion of the right ilium (Fig. 14).

The roentgenologic and clinical diagnosis was Ewing's tumor.

An incision was made over the wing of the ilium and through the muscle. The false capsule of the tumor was incised and there was encountered tumor tissue which was pinkish-white, friable, and so vascular that, after several small pieces were removed, packing was required to control the bleeding.

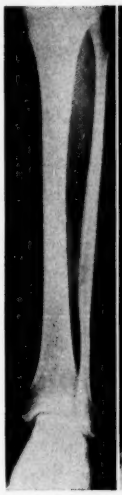
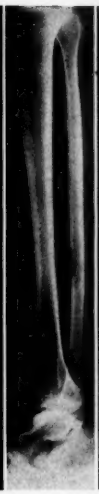
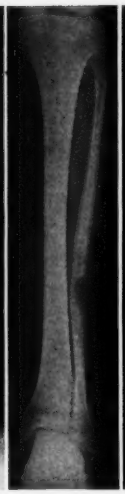

Fig. 8a. Fig. 8b. Fig. 10a. Fig. 10b. Fig. 12. Fig. 13.

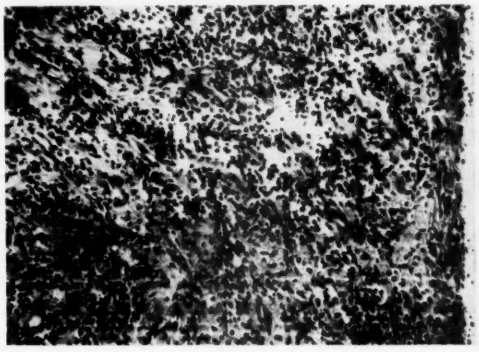
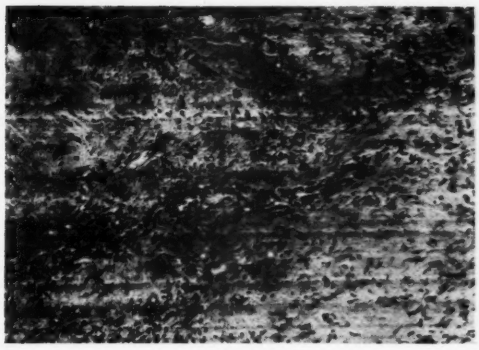

Fig. 9. Fig. 11.

Fig. 8. Case 2. The roentgenogram shows a small area of bone destruction at a point just distal to the middle of the shaft of the fibula.

Fig. 9. Case 2. The photomicrograph shows Ewing's tumor.

Fig. 10. Case 2. The roentgenogram made 40 days after exploration of the fibula and 5 days after the completion of administration of roentgen ray therapy.

Fig. 11. Case 2. Following administration of 1,000 roentgens through each of two portals to the fibula, amputation was done. This photomicrograph of a section of tissue removed from the diseased area shows no cells which can be identified as those of Ewing's tumor.

Fig. 12. Case 2. The roentgenogram of the stump of the femur made more than 9 years after amputation shows no disease.

Fig. 13. Case 2. The roentgenogram of the chest, made more than 9 years after amputation, shows no metastases.

On microscopic examination the cells were found to be fairly uniform with very little cytoplasm and no distinct cell border (Fig. 15). The nuclei were round or oval and basophilic. The chromatin was fairly finely divided. The tumor had extended into the striated muscle. The packing was removed 6 days after operation and roentgen ray therapy was started the next day. Over a period of 27 days, 3,200 roentgens were given through each of 3 portals.

On February 3, 1941, a roentgenogram of the chest (Fig. 16) showed a nodule in the left lung at the level of the second intercostal space and one in the right lung at the level of the third rib. These nodules were thought to be metastatic tumor. No roentgen ray therapy was administered to the chest. Amenorrhea had been present from February, 1941, until August, 1942. A roentgenogram of the chest (Fig. 17) made on October 30, 1941, showed that the

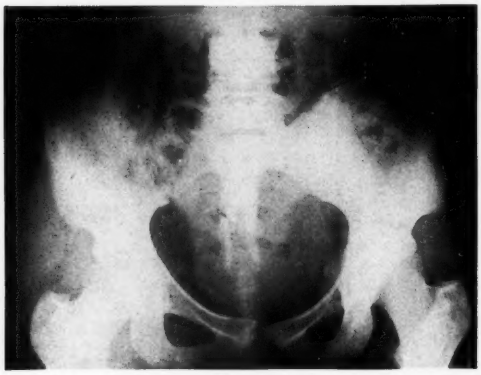

Fig. 14.

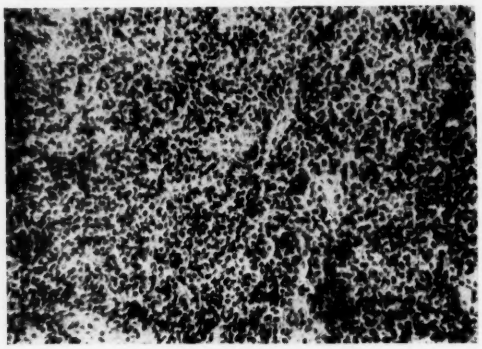

Fig 15.

Fig. 16.

Fig. 17.

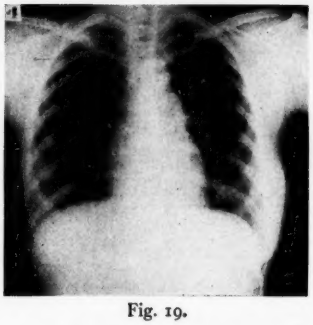

Fig. 19.

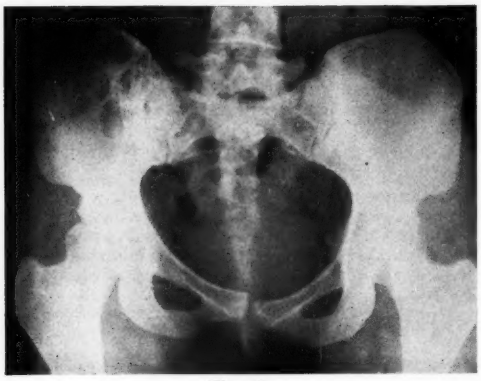

Fig. 18.

Fig. 14. Case 3. The roentgenogram of the pelvis shows an area of bone destruction in the medial portion of the right ilium.

Fig. 15. Case 3. The photomicrograph shows Ewing's tumor.

Fig. 16. Case 3. This roentgenogram was made 5 weeks after the ilium had been explored. There is a nodule in the left lung at the level of the second intercostal space and one in the right lung at the level of the third rib. These nodules were thought to be metastases from the Ewing's tumor of the ilium.

Fig. 17. Case 3. This roentgenogram was made 8 months after the one shown in Figure 16. The nodules are not visible although this patient received no roentgen ray therapy to the chest.

Fig. 18. Case 3. The roentgenogram of the pelvis made 7 years after exploration of the ilium shows no evidence of recurrence.

Fig. 19. Case 3. The roentgenogram of the chest made 7 years after the establishment of the diagnosis of Ewing's tumor shows no recurrence of metastatic nodules.

nodules in the lung had completely disappeared. There was a considerable amount of calcification in the ilium on this date. On September 21, 1944, roentgenograms showed normal lung fields and evidence of bone regeneration in the ilium. In April, 1945, the patient was delivered of a 7 months' infant who lived 6 months. In October, 1947, she was delivered of a 6.5 months' infant who lived only 2 hours. A roentgenogram of the pelvis made on December 4, 1947 (Fig. 18), 7 years after operation, showed that there had been no change in the appearance of the ilium since the film was made in

Fig. 20.

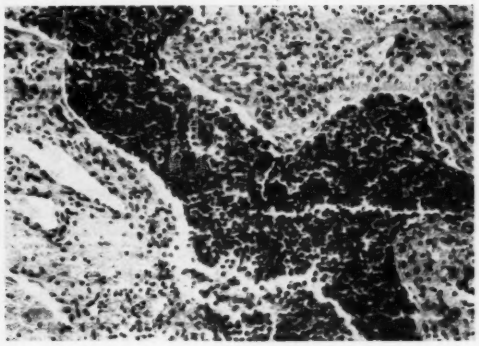

Fig. 21.

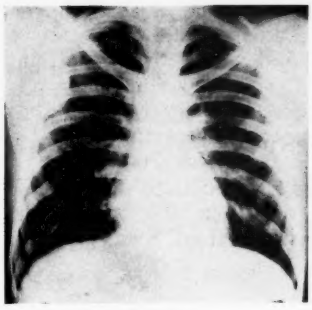

Fig. 22.

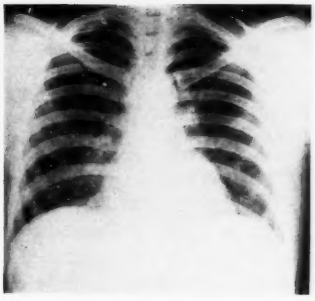

Fig. 23.

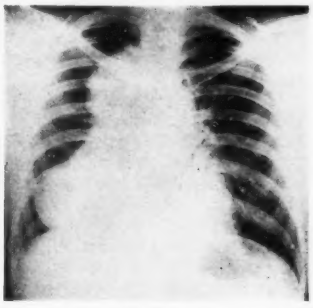

Fig. 24.

Fig. 20. Case 4. The roentgenogram shows areas of decreased and of increased density in the inferior portion of the body of the right ilium and the superior portion of the superior ramus of the pubis.

Fig. 21. Case 4. The photomicrograph of a section of the tissue removed at exploration of the ilium shows Ewing's tumor.

Fig. 22. Case 4. The roentgenogram of the chest shows a nodule near the periphery of the upper lobe of the right lung which was thought to be metastatic from the Ewing's tumor of the ilium and pubis.

Fig. 23. Case 4. This roentgenogram made 9 months after the one shown in Figure 22 shows that the nodule has disappeared. This patient received no roentgen ray therapy to the chest between June 18, 1937 (Fig. 22) and March 29, 1938 (Fig. 23).

Fig. 24. Case 4. The roentgenogram made 3 years after the one shown in Figure 22 shows large masses of metastatic tumor on the right but none at the site of the first apparently metastatic nodule.

1944. There was no evidence of metastatic lesions in the chest (Fig. 19). On March 3, 1948, she was in excellent health. Physical examination showed no evidence of recurrence.

The amazing feature in this patient was the disappearance of lesions which roentgenographically appeared to be metastatic nodules. Except for the diagnostic chest film, the nodules themselves were not irradiated, although the ilium and, evidently incidentally, the ovaries were irradiated. Eight months after their appearance on the film, the nodules disappeared and had not recurred 6 years later. Furthermore, this patient went through 2 pregnancies without reactivation of the disease.

CASE 4. Surg. Path. No. 8785. Not registered with Registry of Bone Sarcoma.

This patient was a white man, 27 years of age, who was admitted to the Vanderbilt University Hospital on March 30, 1937, complaining of swelling of the bladder. One year previously he injured his back and right hip in an automobile accident. The pain in these regions subsided after a few days. Three months before admission to the hospital he began having pain in the right hip and 1 month later he noticed a tender mass in the right lumbar region

which disappeared after a week. Three weeks before admission a mass appeared in the suprapubic region. This mass steadily increased in size.

The temperature was 98 degrees F. and rose subsequently to 100.4 degrees F. In the lower abdomen, extending upward from the pubis, there was a smooth, firm, slightly tender, immovable mass. Rectal examination revealed a mass with similar characteristics. The white blood cell count was 12,400.

A roentgenogram showed that a destructive lesion which involved the medial aspects of the inferior portion of the body of the ilium and the superior portion of the superior ramus of the pubis (Fig. 20).

The clinical diagnosis was tumor of the pelvic bones. The roentgenologist thought that the correct diagnosis was tumor, but stated that the possibility of osteomyelitis could not be ruled out by the roentgenogram alone.

An incision was made near the lateral border of the right rectus muscle and the tumor was exposed retroperitoneally. The tumor tissue was gray, friable, and very vascular. Two pieces of tissue were removed.

On microscopic examination the cells were found to be fairly uniform (Fig. 21). There was a very small amount of faintly eosinophilic cytoplasm, but the cell borders were not distinct. The nuclei were round, basophilic, and contained finely divided chromatin. Small blood vessels were quite numerous.

Six days after operation, roentgen ray therapy was started. Over a period of 17 days a total of 3,200 roentgens was administered through each of 2 portals over the diseased portions of the ilium and pubis.

The abdominal mass decreased in size but did not disappear. On May 20, 1937, a roentgenogram of the chest revealed a large nodule near the periphery of the upper lobe of the right lung. On June 18, 1937, a chest film (Fig. 22) showed that the nodule had increased in size. Although no irradiation was given to the chest except that administered during the 2 diagnostic chest films, the roentgenogram on March 29, 1938, 9 months later (Fig. 23), showed that the nodule had disappeared. On February 4, 1939, no lung metastases were seen on the chest film. On November 1, 1939, a metastatic nodule appeared near the right cardiohepatic angle and on May 29, 1940, several nodules were seen in the right lung, but none in the region where the first metastasis had been seen. Irradiation was administered with some decrease in size of the lesions, but on May 22, 1941, large solid tumor masses were seen (Fig. 24) and roentgen ray therapy was given again. The patient died on October 16, 1941. There never was a recurrence of the nodule that had disappeared without having been directly treated.

The following hypotheses have been considered to explain the disappearances of the pulmonary nodules in Cases 3 and 4:

1. They were not metastatic neoplasms.
2. They were so radiosensitive that the tiny amount of irradiation from the diagnostic chest roentgenography caused them to disappear.
3. Irradiation of the site of the primary tumor activated the cells in the circulation which rendered secondary irradiation to the lungs.
4. Irradiation of the gonads changed the hormonal balance in such a way as to establish conditions which were incompatible with life of the tumor cells.
5. So called Ewing's tumor is not a neoplastic but an inflammatory disease.

SUMMARY

1. The clinical, roentgenologic, operative, and microscopic findings, the treatment, and the results in 20 cases of Ewing's tumor of bone have been described.
2. Three instances of apparent cure of Ewing's tumors have been reported.
3. Two instances have been recorded in which, without direct treatment, apparent pulmonary metastases from Ewing's tumor disappeared.

CONCLUSIONS

1. The bone changes produced by Ewing's tumor of bone and revealed by roentgenography are so variable that a definite diagnosis by that method alone can be made only in the minority of instances.
2. No suspected case of Ewing's tumor should be subjected to irradiation or amputation until microscopic examination of excised tissue has confirmed the diagnosis.
3. It has been possible apparently to cure this disease in 1 instance by amputation, in another by irradiation, and in a third instance by irradiation and amputation.

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THE POSTERIOR SUBSPHINCTERIC SPACE

Its Relation to Posterior Horseshoe Fistula

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EVEN a cursory review of the literature reveals that the superficial variety of anorectal infections has been covered adequately from every standpoint except the anatomic by many well known authorities. Nearly every writer asserts that an intimate knowledge of the anatomy of these related regions is essential, yet few describe these relationships in detail.

For decades it has been recognized clinically that (1) infection of one ischioanal fossa is often followed by infection of the other; (2) this is especially true in neglected cases; (3) as the infection spreads from one ischioanal fossa to the other, it establishes a "posterior horseshoe fistula" in almost every instance. Yet neither the mechanism of spread nor the reason for its location posterior to the anus has been clear. In view of these facts, I shall explain the anatomic relationship of the anorectum as related to posterior horseshoe fistula. The anatomic relationships revealed by my research are in disagreement with the statements made by many previous investigators.

Some have contended that the so-called "anococcygeal raphe," underlying the anococcygeal skin sulcus, forms a definite barrier to the contiguous spread of infection from one ischioanal fossa to the other. This group is inclined to believe that the infection is transmitted by the lymphatics. Nesselrod has confirmed the belief that the lymphatics of this area are intracutaneous and that they are not deep enough to form the basis of a fistulous tract.

Many proctologists have demonstrated clinically the existence of a communicating tract between the two fossae.

From the Anatomical Laboratories of the Graduate School of Medicine of the University of Pennsylvania under the direction of Oscar V. Batson, M.D., Professor of Anatomy; and the proctologic services at Syracuse General Hospital, and Onondago County Tuberculosis Sanitorium.

Others have considered the possibility that this tract was represented in normal anatomy by a surgical space. Hibschman was a proponent of this idea and was responsible for its vogue in Philadelphia.

Several terms, such as the posterior triangular space, the postanal space, and the posterior communicating space, have been used by clinicians to designate collections of areolar tissue in this area. Gorsch and Levy have referred particularly to the posterior triangular and communicating spaces and have defined their limits. Their descriptions and schematic figures appear to be based upon clinical deductions rather than upon detailed dissections.

During the study of the muscles and fascia of the pelvis, several undescribed details bearing on this problem came to light. These are the basis of this report.

RESEARCH MATERIAL

Pelves of 8 human cadavers of the negro and white races, male and female, were dissected in detail. Pelves of 40 cadavers of the negro and white races, male and female, were surveyed in the laboratory while dissected by others. This description is based upon a dissection made from both the perineal and pelvic approach and a comparison of the dissection with sagittal, parasagittal, and coronal sections.

TERMINOLOGY

For clarification, I shall define and limit the following anatomic terms as used in this paper.

Coccygeal muscular raphe. This is a proposed new term to indicate more accurately, the musculo-fibro-tendinous insertions of all three divisions of the inferior layer of the levator (puborectalis, pubococcygeus, and iliococcygeus) into the tip and sides of the coccyx; formerly spoken of as the anococcygeal raphe. The term anococcygeal raphe is a misnomer

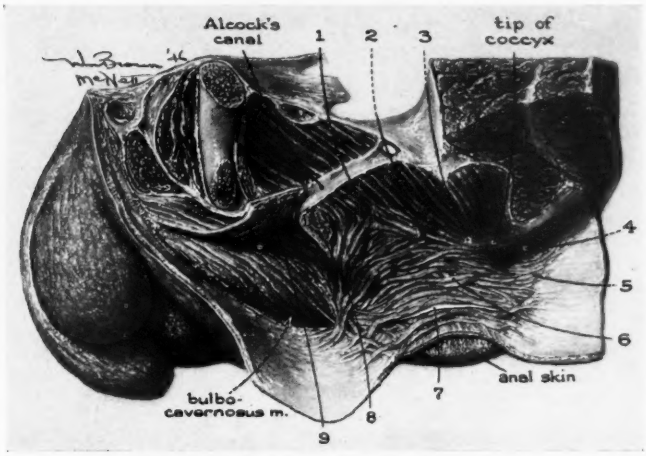

Fig. 1. Lateral view of dissected male pelvis, showing the distribution of the fibers of the levator and external anal sphincter muscles. (Dissection by author.) *1*, Pubococcygeus; *2*, iliococcygeus; *3*, coccygeal muscular raphe, attaching to tip and sides of coccyx; *4*, posterior subsphincteric space, lying between the coccygeal muscular raphe and the coccyx, above, and the posterior insertions of the deep anal sphincter into the skin, along the anococcygeal skin sulcus, below; *5*, posterior insertions of the deep anal sphincter into the skin along the anococcygeal skin sulcus; *6*, deep external anal sphincter muscle, formed from fibers of the puborectalis, as it winds itself around the bowel.

because in no place does this web of muscle fibers attach to, or come in contact with, the anus.

Anococcygeal skin sulcus. This term indicates the groove, crease, or furrow of the skin normally present in the posterior midline of the body, separating the buttocks. It extends from the anus to a variable point over the posterior surface of the sacrum.

Ischioanal fossa. This term, used as a synonym for the ischiorectal fossa, denotes the boundary more accurately, for in no place is this space in relation to the rectum.

ANATOMY

The sphincter muscles and the levator muscle fibers were dissected into their components. By doing this, it was shown that a portion of the fibers of the puborectalis (Fig. 3, *12*), reenforced by fibers of the pubococcygeus (Fig. 1, *1*) and the iliococcygeus (Fig. 1, *2*), forms a flat fibromuscular expanse which inserts into the tip and sides of the coccyx. These combined fibers form the coccygeal muscular raphe of our definition (Figs. 1, *3*, 3, *10*, and 4, *11*).

Just posterior to the anorectum the remaining portion of the puborectalis winds and en-

Fig. 2. Actual close-up photograph of the dissection, as shown in Figure 1. (Dissection by author.) *1*, Pubococcygeus; *2*, iliococcygeus; *3*, coccygeal muscular raphe, attaching to tip and sides of coccyx. *4*, posterior subsphincteric space, lying between the coccygeal muscular raphe and the coccyx, above, and the posterior insertions of the deep anal sphincter into the skin along the anococcygeal skin sulcus, below. *5*, posterior insertions of the deep anal sphincter into the skin along the anococcygeal skin sulcus; *6*, deep external anal sphincter muscle, formed from fibers of the puborectalis as it winds itself around the bowel.

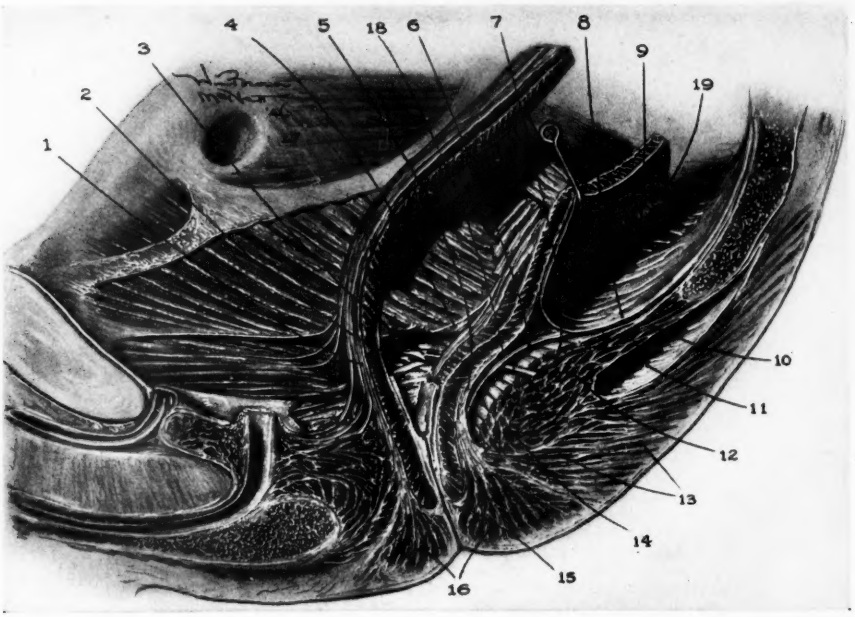

Fig. 3. Drawing showing midsagittal section somewhat schematically, illustrating the relationships of the anorectum to the pelvic diaphragm and the anorectal musculature. A window has been cut through the lateral wall of the rectum, layer by layer, to show the relationships lateral to the rectum. (Dissection by author.) *1*, Combined longitudinal muscle layer (anterior to the rectum). This layer is composed of the longitudinal muscle layer of the rectum, fibers from the levator fascia and fibers from both the superior and inferior layers of the levator. *2*, Inferior layer of the puborectalis muscle. *3*, Arrow lying in the posterior levator space. This space surrounds the rectum like a horseshoe, with the open end of the horseshoe toward the pubis. *4*, Superior layer of the levator muscle. *5*, Combined longitudinal muscle layer of the rectum (posterior to the rectum). *6*, Fiber from the superior layer of the levator, to the combined longitudinal muscle layer of the rectum. *7*, Inferior boundary of the posterior levator space formed behind the rectum by the superior surface of the coccygeal muscular raphe. *8*, Iliorectococcygeus muscle formed by fibers from the iliococcygeus (striped), fibers from the longitudinal muscle layer of the rectum (smooth), and a few fibers from the levator fascia. This muscle forms the superior boundary of the posterior levator space behind the rectum. *9*, Retrorectal space. *10*, coccygeal muscular raphe, attaching to the tip and sides of the coccyx. *11*, Posterior subsphincteric space (connecting the two ischioanal fossae) bounded anteriorly, by the posterior surface of the deep external anal sphincter, superiorly, by the inferior surface of the coccygeal muscular raphe, and inferiorly, by the decussating fibers of the deep portion of the external anal sphincter as they insert into the skin. *12*, Puborectalis muscle (the sling of the puborectalis behind the rectum). *13*, Fibers of the deep external anal sphincter muscle inserting into the skin along the anococcygeal skin sulcus. *14*, Deep external anal sphincter muscle (posterior to the rectum). *15*, Anal intermuscular septum.

twines itself around the bowel to form the deep external sphincter muscle (Figs. 1, *6*, 3, *14*, and 4, *9*). Some of these puborectalis fibers split off and form a flat web which lies inferior to the coccygeal muscular raphe. The fibers of this web, which are the posterior insertions of the deep external sphincter, lie just beneath the skin of the anococcygeal skin sulcus and terminate by inserting into this skin (Figs. 1, *5* and 3, *13*). Between these superficial and deep muscle extensions, there is a thin mass of fat and loose connective tissue which extends to either side and is there continuous with the fat and areolar tissue of the ischioanal fossae.

This potential fat filled space, for which I propose the descriptive, anatomic name "The posterior subsphincteric space" (Figs. 1, *4* and 3, *11*) is situated between the muscular wall of the anal canal in front and the coccyx be-

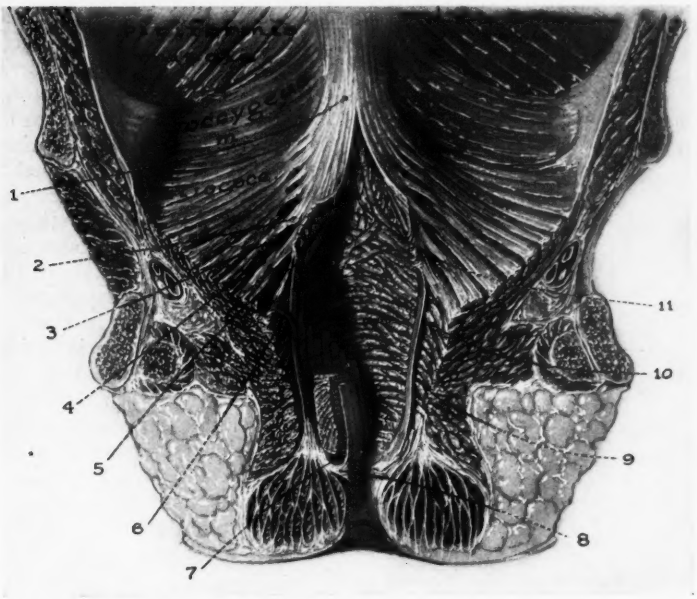

Fig. 4. Drawing showing the coronal section of a dissected male pelvis somewhat schematically, illustrating the extent of the posterior levator space posterior to the rectum, and the manner in which the inferior layer of the levator winds itself around the rectum to form the deep external sphincter muscle of the anus. The iliorectococygeus muscle has been split in the posterior midline and the flaps turned upward. The wall of the posterior half of the rectum has been removed, with the exception of a few muscle bundles of the combined longitudinal muscle layer on each side and a block of the lower end of the internal sphincter muscle on the right. The skin of the anal canal has been removed. (Dissection by author.) *1*, Iliorectococcygeus muscle; *2*, superior layer of the levator; *3*, inferior layer of the levator; *4*, levator muscle (lateral to the point of division into a superior and an inferior layer); *5*, muscle bundle from the superior layer of the levator to the combined longitudinal muscle layer of the rectum; *6*, muscle bundle from the inferior layer of the levator to the combined longitudinal muscle layer of the rectum; *7*, circumanal space; *8*, anal intermuscular septum; *9*, deep external anal sphincter muscle; *10*, puborectalis muscle showing the inferior layer as it winds and entwines itself around the bowel to form the deep external anal sphincter muscle; *11*, coccygeal muscular raphe (inferior boundary of the posterior levator space behind the rectum).

hind. On sagittal section the shape of this space varies somewhat, depending upon whether the section is made through the anococcygeal skin sulcus or at points lateral to it. The narrowest part of the space is found by section through the midline of the body (through the anococcygeal skin sulcus) in which plane the space is irregularly elliptical in shape. The actual photographs and drawings give a better idea of the space than the description. In anatomic terms, however, the space may be said to be bounded anteriorly, by the posterior surface of the deep external anal sphincter (Figs. 1, *6* and 3, *14*), superiorly, by the inferior surface of the coccygeal muscular raphe (Figs. 1, *3* and 3, *10*), and, inferiorly, by the decussating fibers of the deep portion of the external anal sphincter as they insert into the skin (Figs. 1, *5* and 3, *13*). Actually, these several muscle components are derivatives or extensions of the puborectalis muscle.

This posterior subsphincteric space (1, 2, 3, 4) lies in the exact location of posterior horseshoe fistula. It appears then, that this fistula represents the extension of an infection by contiguity.

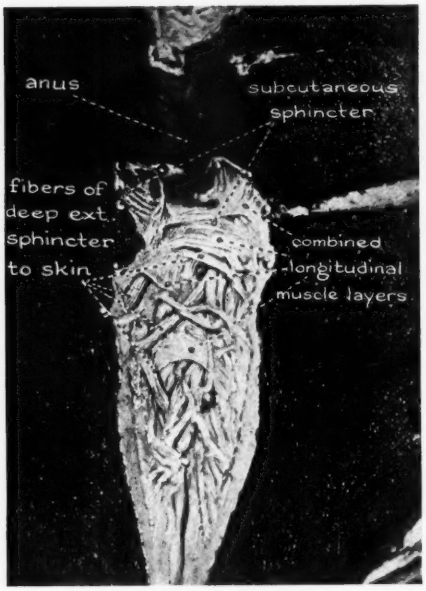

Fig. 5. Photograph showing the insertions of the subcutaneous sphincter, the deep sphincter, and fibers from the combined longitudinal muscle layer of the rectum into the skin along the posterior midline. An incision has been made through the skin in the midline (anococcygeal skin sulcus) and extended into the anal canal. The skin edges have been pulled apart and held in place by pins. (Dissection by author.)

SURGERY

Muscles, including their origins and insertions, must be preserved whenever possible if one is to secure the best functional result. In the majority of cases it is unnecessary to make the usual horseshoe-shaped incision, passing around the anus posteriorly, to cure this type of fistula. Curvilinear incisions are made lateral to the external sphincter muscle over the most prominent part of the ischioanal abscess on either side. These incisions are carried anteriorly to the full extent of the abscess cavity and are terminated posteriorly at the lateral margins of the insertion of the anal sphincter into the skin. If a Penrose drain is passed from one incision to the other, through the posterior subsphincteric space, adequate drainage will be secured. The preservation of the posterior insertion of the anal sphincter into the skin prevents unnecessary loss of sphincter control and the horrible deformity often seen following the use of the horseshoe incision. The lateral incisions must be extensive and the wounds saucerized. However, when the deep spaces are involved (the posterior levator, the retrorectal, and the lateral pelvirectal spaces), it sometimes becomes necessary to make the horseshoe incision in order to follow the deep portion of the fistula tract and to secure proper exposure and drainage of these deeper spaces. In these cases, it is far better to sacrifice the insertion of the anal sphincter into the skin than the insertion of the levator into the tip and sides of the coccyx. Whenever this is necessary, the incision posterior to the anus should be made well up over the coccyx and a flap of skin, including the insertion of the sphincter muscle into it, should be reflected forward until the posterior subsphincteric space is reached.

SUMMARY

Dissection of a series of cadavers has shown a definite, fatty, areolar tract joining the two ischioanal fossae. This tract lies posterior to the anus and between two prolongations of the puborectalis muscle. The location of this space coincides with the location of posterior horseshoe fistula.

CONCLUSION

Since a knowledge of the presence, location, and limitations of every potential space is essential to fistula surgery, and since there has been much confusion as to the exact pathway of posterior horseshoe fistula in the past, it is hoped that this paper will be of some value in clarifying this situation in the future.

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THE CRITERIA, CLASSIFICATION, AND TECHNIQUE OF ILIOPECTINEAL (COOPER'S) LIGAMENT HERNIOPLASTY

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THE acquisition of knowledge of the surgical treatment of hernia entails, among other things, an acceptable yet practicable classification of hernial operations. In a previous publication mention has been made of three major classifications of hernial operations, namely, herniotomy, herniorrhaphy, and hernioplasty. It is not proposed to discuss further herniotomy or herniorrhaphy but we would like to clarify the current conception of hernioplasty. With the universal acceptance of iliopectineal (Cooper's) ligament repairs, hernioplasty has become more inclusive. Currently it connotes a greater scope of plastic variants than it did a decade or so ago when repairs were confined almost exclusively to the use of the inguinal ligament as anchorage for the separated fascial boundary. The recognition of two types of hernioplasty, inguinal ligament hernioplasty, and iliopectineal (Cooper's) ligament hernioplasty, has been helpful and an advance-step in lessening misunderstanding when referring to these plastic reparative procedures. The technical development of the former, with the use successively of fascial sutures, of free ore pedicled fascial grafts, of pedicled muscle grafts, and recently of cutis grafts, constitutes one of the most interesting chapters in the progress of hernial surgery. Furthermore, it seems likely that the cumulative story of the progressive evolution of various maneuvers employed in iliopectineal ligament repairs will ultimately be equally as fascinating.

The purpose of this paper is: (1) to focus attention on some of the factors which have played a role in retarding the development of the various maneuvers in Cooper's ligament repairs; (2) to present a practical classification and the criteria for each variant; and (3) to describe and illustrate the technique of the combined operation.

From the Veterans Administration Center.

In recent years there has been a rising interest in and a general acceptance of iliopectineal ligament hernioplasty, which has been reflected in an increasing number of articles appearing in the literature on this technical aspect of hernia repair. As a result of this transition in technique, the successive variants employed for implementing the coexisting anatomical weaknesses have become standardized and correlated so that the composite operation is rapidly approaching the position of challenging the choice of the inguinal ligament in the repair of certain types of inguinal hernias. In retrospect, it is difficult to understand why anyone familiar with the anatomic relationships in the inguinofemoral region and the dynamics of the progression of the hernia, could overlook for long the inherent advantages of a deeper parietal anchorage and a mechanically better shunting angle to intra-abdominal force which obtain in iliopectineal ligament repairs.

The chief factors which may be considered as playing a contributing role in the reluctance of surgeons to take advantage of this valuable and, for the most part, easily accessible ligament are:

1. *The failure of technical progress to keep pace with anatomic knowledge.* Progress in surgery is not wholly dependent on anatomic knowledge, but, sharing importantly in its progress is the ability to recognize discernible technical pitfalls and on the increasingly efficient application of ways of correcting congenital or acquired deficiencies. The latter prerequisite imposes the necessity of constant acquisition of new information. Moreover, we should realize that during the evolution of the modern concept of hernia repair, which had its inception only a half-century ago, the opportunities for surgical training in herniology were far less than in the present day of industrialization in which operative repair of hernia is universally accepted as the treatment of

choice. In the former era of surgery, hernias were not operated on unless they became strangulated or reached a size incompatible with gaining a livelihood; while in the present era many hernias are repaired that were previously unrecognized by the individual and were only discovered during a pre-employment examination or on induction into military service. Consequently, the opportunity for surgical experience in the treatment of hernia in its incipiency, as contrasted with the prevalent scrotal hernia of a half-century ago, has increased manifoldly. Moreover, during this interim there has been a decided trend toward internal or deeper repair by the correction of the saccular weakness intraperitoneally and the use of Cooper's ligament as anchorage for the wall, in contrast to the former practice of extraperitoneal removal of the sac, reinforcement of the anterior layers of the wall and the employment of the inguinal ligament as the sheet anchor.

2. *The erroneous but prevailing concept of the origin and eradication of the femoral variant of the sac.* Because of earlier reports of the low incidence of recurrence of femoral hernias repaired by the inferior or femoral approach, a technique which precludes total removal of the sac, surgeons generally gained the erroneous idea of the efficacy of this technique. It did not occur to them to challenge the technique on anatomical grounds or to analyze and re-evaluate the source of the statistical data which were obtained from small series of patients operated upon and from what is currently recognized as incomplete follow-up records. It is therefore not surprising that there has been professional resistance to any suggestions for alteration of the conventional technique of saccular ligation from below, usually implemented by the suturing of the inferior margin of the inguinal ligament to the pectineal fascia or occasionally to Cooper's ligament, a technique which had been in effect for a quarter of a century. Statistical surveys of the last decade have shown that the inguinal approach is favored over the femoral and coincidentally with decreasing incidence of inguinal and femoral recurrences. McClure and Fallis (1939) in their series of 90 femoral hernias found that 22.3 per cent had been operated on previously for inguinal hernia on the same side. These findings suggest that the patients were subjected to two operations because of a diagnostic error or that more than casual relationship exists between femoral and inguinal hernias.

The superiority of the inguinal route lies in providing: (1) greater accessibility to the sac and its variants; (2) better definitive exposure of the wall adjacent and remote to the defects in the floor of the canal as well as those occurring in the interligamentous space; (3) more accurate evaluation of the composite weaknesses and of the neighboring structural integrity; and (4) complete visualization of the iliopectineal ligament and trihedral space. Consequently, the superior approach has increased the anatomical frontiers of the congenital and distortional weaknesses of the inguina and coincidentally has extended the surgical horizon of hernia repair. This composite concept of inguinofemoral herniation provides the resourceful surgeon with a wider range of ingenious maneuvers for augmenting the combined inguinopectineal or three dimensional repair. Simultaneously with the almost universal acceptance of the principle of retrogressive mobilization and conversion of the various locules into the parent sac before total exsection, there has come a revival of the concept of triangulation of the inguina which was originally proposed by Hesselbach in 1806. Ferguson, and Andrews and Bissell recognized the importance of the smaller internal inguinal triangle in the development of incipient direct hernia, and emphasized the necessity for reinforcing the wall overlying the internal fossa in the prevention of recurrences of this type of hernia.

Ordinarily we are prone to think only of the urogenital and vascular orifices in or adjacent to the floor of the canal as sources of the hernia, overlooking the other rare but equally important congenitally susceptible mural or ligamentous weaknesses. Yet, in Cooper's book, published in 1804, there is a plate depicting 6 such orifices. Anatomically and surgically there is currently recognized 12 or more actual or potential areas of weakness through which herniations have occurred. It would therefore seem logical for the purpose of exactness of

their location to describe them in relation to the triangles of the inguina. Burton and Dugdale have revived and extended this idea by considering the entire hernia-bearing region as a composite unit or the inguina. Each inguen is triangularized by dividing it into: (1) a major superior triangle, which lies anteromedial to the inguinal ligament and comprises Hesselbach's and a medial triangle; and (2) a major inferior triangle which is inferomedial to the inguinal ligament or trihedral space. It consists of the lesser vascular and the muscular triangles, respectively. Therefore, by correlating the saccular and triangular relationship one can better understand the validity of the retrogressive removal of the saccular variants and better define adjacent structural elements preparatory to the creation of barriers to prevent recurrence of the herniation.

Unfortunately, in descriptions of inguinal and femoral hernias, so complete has been the regional bias that each area has usually been discussed with little regard to the anatomical relationships or the continuities of the fascial layers therein.

3. *Failure explicitly to set forth criteria for iliopectineal (Cooper's) ligament hernioplasty.* Experience gained from contact with the resident staff has revealed that they seldom have any preconceived idea as to what structural deficiencies or parietal distortions warrant the use of the iliopectineal ligament in hernia repair. There is a common tendency, which is a valid one, to employ it in all refractory hernias; included in this category are most preternaturally large recurrent hernias. They are confounded as to what saccular variants or precise structural deprivations constitute the indications for a Cooper's ligament repair. This lack of complete understanding of the relationship of the various anatomical weaknesses is due in part to the paucity of the literature on this etiologic aspect of hernia but is many times traceable to the delinquency of the senior surgeons who have inadvertently failed to point out the reasons for the application of this progressive step of employing the iliopectineal ligament in the radical treatment of hernia.

The criteria for the employment of Cooper's ligament may be classified as absolute and equivocal. The absolute are: (a) all femoral loculations of the sac and (b) inadequacy of the inguinal ligament. The equivocal indications are: (a) multiple coexisting saccular locules; (b) generalized parietal laxity of the inguina; (c) fascial incompetency, which not infrequently is associated with aponeurotic or interfascicular defects; (d) refractory hernias or the presence of any marked distortional anatomical pattern as obtains in plural recurrencies; (e) certain extrinsic factors such as the constitutional habitus and particularly those individuals suffering from asthmatic bronchitis or chronic recurring coughing paroxysms. It is realized that some of the correlative indications enumerated in the equivocal group fall within that controversial frontier which is only measurable by surgical experience.

CLASSIFICATION OF ILIOPECTINEAL LIGAMENT HERNIOPLASTY

The hernia-bearing region of either lower abdominal quadrant is commonly referred to as the inguinal region and less frequently as the groin. This large triangular area is bounded by the inguinal ligament, the rectus sheath, and the ilioumbilical line with the pubic spine as its apex (3). Such an anatomicosurgical concept envisages herniations through the floor and cranial portion of the canal as well as spontaneous hernias in the semilunar and semicircular lines (spigelian). The other triangular component which is more deeply placed lies inferior and medial to the inguinal ligament with Cooper's ligament as its deeper boundary and the spinoeminential line, its superior limit, is known as the inferior inguinal region, interligamentous or trihedral space. Similarly, the composite superior and inferior inguinal regions are designated the inguina. By the foregoing triangulation of the inguina there is more accurate orientation and correlation of the various saccular and structural departures.

Surgeons have long searched for a single anatomic approach through which all protean weaknesses of the inguina can be corrected. Such a route should fulfill the following prerequisites: (1) afford adequate exposure to meet any contingency that has developed in

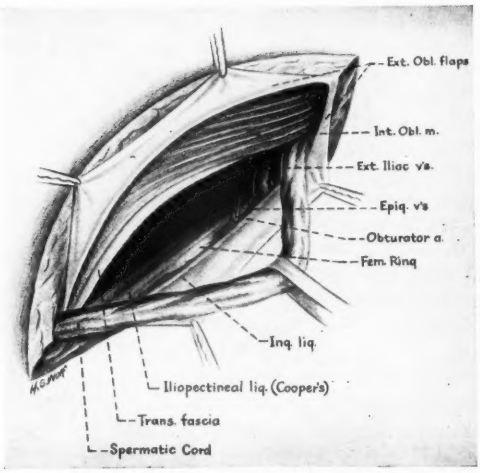

Fig. 1. The anatomy of the inguen is illustrated depicting the important anatomical structures which are encountered in performing the combined inguinopectineal repair. Attention is called to the relationship of the inguinal and iliopectineal relationship of the inguinal and iliopectineal (Cooper's) ligaments. The epigastric vessels which lie in the superior triangular space are constant and are routinely ligated. The obturator vessels are frequently anomalous but their most frequent relationship is shown, which is in the inferior triangular space. They cross the superior pubic ramus juxtamedial to the external iliac vein and when in this position are routinely ligated. The ligation of these vessels exposes the iliopectineal ligament to the level of the external iliac vein, so that wide anchorage of the parietal wall to this ligament is possible.

the progress of the hernia or which may arise during the course of the operation; (2) possess flexibility in dealing with definitive and congenitally susceptible weaknesses; (3) facilitate saccular exsection inclusive of aberrant locules; and (4) permit leeway for the exercise of ingenuity of the surgeon in the creation of a deeply placed unyielding floor. It is our contention that the inguinal approach of Lotheissen meets all the requirements as outlined for the employment of the iliopectineal ligament in hernia repair. However, because of the frequency of diverse and occasional anatomic or embryonic inguinofemoral weaknesses which may coexist, this foundational approach to all inguinal triangles makes possible many intrinsic maneuvers for augmenting definitive mural, intraligamentous or interligamentous defects. These technical variants have been classified according to their evolutional development into: (1) femoral hernioplasty, (2) pectineal hernioplasty, (3) inguinopectineal hernioplasty, and (4) combined inguinopectineal hernioplasty.

1. *Femoral hernioplasty.* This technical procedure was the first evolutional step in the departure from the conventionally used inguinal ligament. It constitutes the simplest type of Cooper's ligament repair. The technique was originally proposed by Sir Astley Cooper but it was Annandale in 1876 who made practical application of it. Ruggi in 1892 advocated its employment routinely in all femoral hernias. The operation entails ligation of the femoral locule, followed by either occluding the femoral ring with a plug of redundant tissue or by its direct closure by suturing the anterior margin of the ring to Cooper's ligament. The normal relationship of the cord or parietal structures are not disturbed. Like other maneuvers there are certain limitations imposed on this procedure: The hernia must be exclusively femoral, and there must be no coexisting mural weakness. Unfortunately, these criteria seldom exist alone. The operation is the counterpart of the early inguinal herniotomy of Ferguson in which the indirect locule is ligated but the floor of the canal is not mended and the position of the cord is not altered.

It should be an unvarying rule in every hernia operation to expose the peritoneum at the internal ring first. From this pivotal point, all saccular variants are successively mobilized. The presence of a femoral loculation is an absolute indication for iliopectineal repair. It differs from the indirect locule in its location and the fact it does not arise from a vestigial remnant. Its site of exit is through the velamentous fascia in the interligamentous space and usually through an enlarged femoral ring. By tracing intraperitoneally the origin of the different variants of the sac, it has been observed that the femoral outpouching arises from the inferior convex portion of the direct component of the sac. Ordinarily with the intraperitoneal approach the femoral protrusion and its fatty envelope can be easily withdrawn through the femoral ring. If the hernia is incarcerated it may be necessary to section the lateral margin of the lacunar ligament

which will facilitate intrapelvic delivery of the incarcerated mass. After the femoral locule is inguinalized the direct component of the sac is freed and indirectalized. This retrogressive procedure of mobilizing the sac intraperitoneally and intrapelvicly is of imminent importance but unfortunately this technique of total saccular extirpation is not universally followed.

The infraligamentous approach to a femoral hernia has many disadvantages: (1) it provides accessibility only to the femoral variant of the sac; (2) it is not possible through this route digitally to examine the sac for other communicating locules which frequently coexist; (3) there is greater likelihood of injuring incarcerated bowel or if it should be suddenly released the surgeon may not be able to ascertain its viability before it disappears into the general peritoneal cavity; (4) a total exsection of the femoral locule is more difficult; (5) should a loop of incarcerated bowel become gangrenous, its resection and anastomosis of the viable ends as advocated by Dennis and Varco could not be done through the inferior exposure.

The second maneuver in femoral hernioplasty is the closure of the ring. This is done by bringing the anterior margin of the ring, which is the inferior edge of the inguinal ligament, down to the iliopectineal (Cooper's) ligament by means of either a silk or a living fascial suture. If the femoral ring is dilated and the inguinal ligament unyielding, precluding its apposition to Cooper's ligament without tension, a fascial suture is preferable. Carscadden and Payne adapted the principle of McArthur by using a strip of external aponeurosis as a suture to bridge the annular defect. A Gallie free fascia lata suture serves equally as well. Dowden contends that the walls of the femoral ring are too rigid to be amenable to sound and reliable approximation. He therefore proposed buttressing the ring by suturing the bunched-up stump of the sac, properitoneal fat or omentum, so as to overlie and occlude the entrance to the canal. The prototype of this technique was employed to occlude the internal abdominal ring by Macewen in 1886 and McEwen in 1890 but was subsequently abandoned.

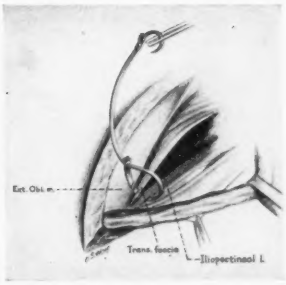

Fig. 2. The first fascia lata suture is started, showing it autotransfixed after passing through the edge of the medial aponeurotic flap and the fascia transversalis and through the iliopectineal ligament near the inguinopectineal juncture, posterior to the pubic spine.

Because of its limitations, femoral hernioplasty without implementing it with some other maneuver is rarely employed.

2. Pectineal hernioplasty. This operation consists of two steps. The first entails the removal of the sac inclusive of all its locules; the second entails the exclusion of the femoral ring and the repair of the wall by suturing the fascia transversalis alone, or jointly with the other parietal strata, to the iliopectineal (Cooper's) ligament, starting deep to the pubic spine and continuing to the medial border of the external iliac vein.

In the presence of a coexisting saccular and mural hernia, additive reparative measures are called for. The sac is first disposed of in the conventional way. When the parietal insufficiency of the floor of the canal is chiefly of the atonic type, a special effort is directed toward taking up the slack by the creation of a deeply placed wall, which is also strategically more secure. By the utilization of Cooper's ligament as anchorage, the angle of diversion of the wall with the pelvis becomes more acute, thus lessening the concavity of the inguinal fossae; coincidentally there is early shunting of the intra-abdominal thrust. Figures 2 and 3 depict the attachment of the fascia transversalis and medial aponeurotic flap jointly to the iliopectineal ligament with a living fascial suture. The suture begins posterior to the pubic spine and progresses lateralward to the medial border of the iliofemoral vein. This point is usually marked by a minute bony ridge paralleling the vessel or less

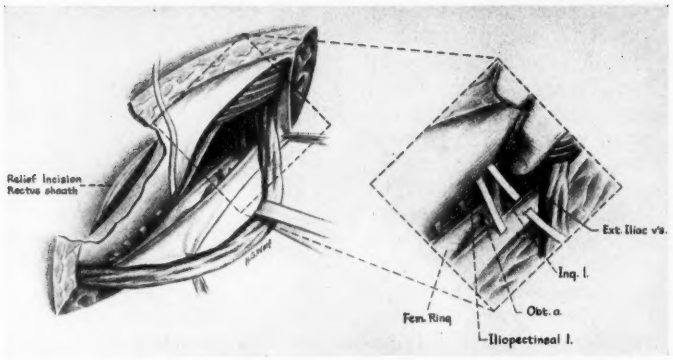

Fig. 3. The first fascial suture has progressed from the caudal end of the iliopectineal ligament to the external iliac vein where it alters its direction, leaving the iliopectineal ligament and becoming more superficial. From this transitional point it passes through the parietal wall (internal and external oblique) and through the inguinal ligament successively to the newly placed external ring which now lies cephalad to the internal abdominal ring. The cord is displaced with concomitant reversal of the obliquity of its transparietal portion. A relief incision medially placed in the anterior rectus sheath is occasionally necessary to release undue tension on the fascial suture. The insert shows in greater detail the placement of the suture at the transitional space.

frequently by a small eminence on the superior pubic ramus. At this juncture, the suture changes its direction and passes from the iliopectineal ligament through the inferior margin of the inguinal ligament. It continues successively through the internal-external oblique strata and the inguinal ligament to the external ring. In this technique the external ring is reversed and occupies a position cephalad to the internal abdominal ring. The cord is transposed extra-aponeurotically. It should be noted that in the placement of this suture the wall is moved medial and deep to the femoral ring and interligamentous space.

A prerequisite to a pectineal hernioplasty is an available, competent fascial stratum. In the event the fascia transversalis becomes stretched, the medial denser portion near its conjunction with the rectus sheath may be brought down to the ligament. Should this maneuver cause undue tension of the fascia, a vertical or curved incision through the anterior rectus sheath, as suggested by Fallis and Tanner, respectively, will permit sufficient fascial separation without predisposing to any underlying weakness to relieve the abnormal tautness of the fascia transversalis. In our experience the Gallie fascial suture is ideally suited for this step of the repair. The suture is easily obtainable, strong, somewhat elastic, nonirritating, lasts many years, produces broader contacting surfaces and its placement is accompanied by minimal trauma.

3. Inguinopectineal hernioplasty (closure of the interligamentous space). The interligamentous, inguinopectineal or trihedral space lies between the inguinal and iliopectineal ligaments and the anterior abdominal wall. Its superior limit is the internal ring and it extends inferiorly to the pubic spine. As a potential source of weakness this space has received only passing attention. In the conventional or classic hernia operation this vulnerable area is usually given little consideration. In modern textbooks of surgery no mention is made of the importance of reinforcing the velamentous fascia of this space or of stabilizing the inferior edge of the inguinal ligament. Statistically there are no reports incriminating this area as a possible cause of recurrent herniations other than femoral ring; yet, not infrequently one encounters a diffuse bulging through this subinguinal space. This singular lack of recognition or its proper evaluation in hernia repair is explained on the ground there is no classification for

herniation through the interligamentous space unless it is considered a variant of femoral hernia. The only exception is Wilmoth's classification of femoral hernia into prevascular, pectineal, translacunar, and multidiverticular. Too often, we are prone to think of femoral hernia as coming through only the femoral ring rather than bulging through the inguinopectineal space.

The idea of closing the interligamentous space is not new. Fabricius (19) divided the inguinal ligament to facilitate its approximation to the pubic ramus. Subsequently this principle was revived by Litsitsyn and Cheever who modified it by staggering the sectioning of the ligament. While there is concurrence in the objective to be attained by this maneuver, nevertheless the repair of such a strategically important structure as the divided inguinal ligament is an objectional feature which is almost as serious as the correction of the initial weakness. This perhaps accounts for the paucity of surgeons using this departure in technique. Moschcowitz in 1907 popularized the earlier novel idea of Ruggi of obliterating the interligamentous space by suturing the recurved portion of the intact inguinal ligament to the iliopectineal (Cooper's) ligament but omitted the previous objection of cutting the former. Since Cooper's ligament is a constant fixed structure of unvarying density, success of the Moschcowitz operation is dependent upon the pliability of the inguinal ligament, permitting it to span this vulnerable space. The pitfall of this technique is the tendency forcibly to displace a tense inguinal ligament in an endeavor to close the interligamentous space, unmindful of the fact that the maneuver is unphysiological and frequently results either in tearing the ligament or in cutting through of the silk sutures. Too often the ultimate outcome is the return of the sutured structures to their former position. To obviate this objectional feature an autogenous fascial suture may be interlaced between the ligaments, in effect to form a permanent fascial barrier (Fig. 5a).

Another simple but effective method of reinforcing the interligamentous space is the reflection of the lateral aponeurotic flap medialward and inferiorly. Ordinarily the flap is

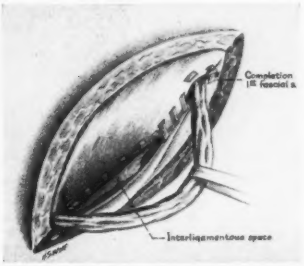

Fig. 4. The first fascial suture has been laid. It may or may not encircle the cord at the external ring, depending upon its length and the preference of the surgeon. The space between the inferior edge of the inguinal ligament and Cooper's ligament (interligamentous space) has not been obliterated. By attaching the parietal wall well laterally so that it is contiguous with the external iliac vein, the femoral ring is excluded and lies superficial to the first imposed parietopectineal barrier.

of sufficient width to allow its edge to be sutured to the iliopectineal ligament without tension (Fig. 5b). The converging medial and lateral aponeurotic flaps which are anchored to the iliopectineal ligament producing a narrow gutter superjacent to the ligament. By suturing the adjacent surfaces of the aponeurotic flaps, the depression will be smoothed out and the wall further strengthened. This method of obliterating the interligamentous space is technically easier, more physiological and since there is fascia-to-fascia contact it lessens the need for a living suture.

In placing the inguinopectineal hernioplasty in its proper perspective in relation to allied maneuvers, it would seem rational to use it as an adjunctive rather than a basic maneuver.

4. Combined inguinopectineal hernioplasty. (*The composite operation or three dimensional repair.*) The preceding variants in technique have been successful when measured in terms of comparative results and invaluable in contributing to the progressive security of the wall. But, each maneuver was designed to correct a specific anatomical deficiency and consequently they each have their limitations. It is not uncommon for the surgeon to be confronted with plural and varied weaknesses coexisting in the superior and inferior inguinal triangles, the correction of which no single technical maneuver would suffice. An analysis of the criteria for the various maneuvers has led to the conclusion of proposing a composite

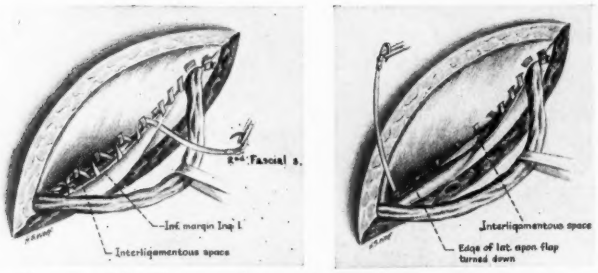

Fig. 5. a, left, The second step of combined operation has for its objective the closing or reinforcement of the interligamentous space. It begins with the placement of second fascial suture which passes through the loops of the first fascial suture and through the inferior edge of the inguinal ligament running from the pubic spine laterally to the transitional angle. The suture serves as a living fascial barrier, in the event the inguinal ligament is taut and cannot be apposed to the iliopectineal ligament. b, The second fascial suture starts at the pubic spine but anterior to the first, going through the first loop of the first fascial suture and through the turned down edge of the lateral aponeurotic flap.

operation compounding the advantages of the several standardized technical variants employed in the evolution of Cooper's ligament repair.

TECHNIQUE OF COMBINED OPERATION

Certain cardinal principles, such as mobilization and excision of all locules of the sac and defining the anatomical structures of the floor of the canal are commonly agreed upon by all surgeons preparatory to proceeding with the repair. Therefore, these preliminary features of the operation will be omitted from the description. An inguinal approach is used. The first step of the composite operation is identical with pectineal hernioplasty. As suture material we prefer two fascia lata strips as described by Gallie and LeMesurier. Strategically, this is considered the most important maneuver of the operation for, if this defense barrier fails to hold, the subsequent adjunctive maneuvers are jeopardized. Attention is drawn to certain minor technical departures which will shorten the operating time without compromising the integrity of the wall. In our earlier experience only the fascia transversalis was apposed to the iliopectineal ligament. It was recalled that Joyce sutured the fascia transversalis and medial aponeurotic flap, jointly as one stratum, to the recurved portion of the inguinal ligament. He reported an enviable recurrence rate using this technique. We simply adapted the principle of Joyce but substituted the iliopectineal ligament for the inguinal ligament.

The first fascial suture passes through the fascia transversalis and medial aponeurotic flap and then through Cooper's ligament respectively (Fig. 2), which is continued in this manner to the external iliac vein. The vein is displaced and protected with the finger on placement of the last suture in Cooper's ligament (Fig. 3). At this point the fascial suture changes its direction, which is at the level of the iliac vein where it crosses Cooper's ligament and runs obliquely cephalad, passing through the inguinal ligament and parietal strata to the newly created external ring. In effect, this closure reverses the obliquity of the transparietal portion of the canal. The transition from the iliopectineal ligament to the inguinal ligament is of crucial importance for it is the most frequent site of recurrence in this type of repair. It is therefore essential that great care be exercised in the placement of the transitional suture as it passes through the adjacent strategic structures: the parietal wall, iliopectineal and inguinal ligaments, respectively (Fig. 3). Since this is a triangular space a continuous or figure-of-eight suture is superior to interrupted sutures. Moreover, because of easy compressibility of the external iliac vein, which conceivably could occur from intra-abdominal pressure, it is obvi-

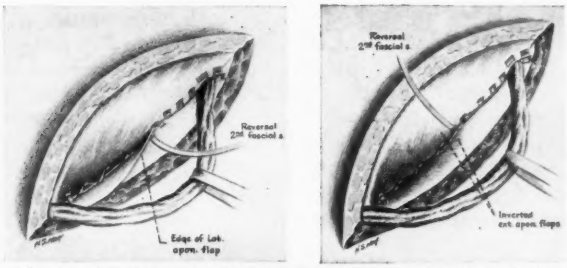

Fig. 6. a, left, The second fascial suture is reversed and imbrication of the lateral aponeurotic flap begun. It passes through the edge of this flap and through the ventral surface of the medial. b, The second fascial suture continues cephalad passing through the same structures, which pulls the lateral aponeurotic flap down to the iliopectineal (Cooper's) ligament. This maneuver obliterates the interligamentous space from the pubic spine to the medial border of the external iliac vein where the suture is reversed.

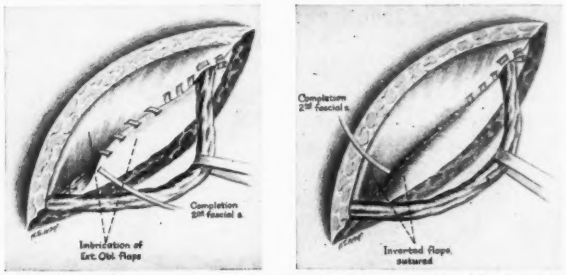

Fig. 7. a, left, Completion of second fascial suture. In this three dimensional repair there is reinforcement of the floor which is more deeply placed, implemented by closure of the interligamentous space. The cord is transposed extraaponeurotically and the transparietal portion points cephalad. b, The second fascial suture has been reversed and runs caudally through the ventral surfaces of the inverted medial and lateral aponeurotic flaps, which eliminates the gutter suprajacent to the superior pubic ramus and completes the all-fascial closure. The cord is placed extra-aponeurotically.

ous that the potential vulnerability of this space cannot be totally eliminated.

In the placement of the first fascial suture, which is the first step of the combined operation, it is essential to have adequate exposure of Cooper's ligament. Routinely ligating the epigastric vessels and also the obturator vessels when present will be helpful. An ingenious maneuver has been described by Rees in which the direction of the femoral vein is changed from 15 degrees inward to 35 degrees outward by abduction of the hip. It would facilitate the placement of the lateralmost and deepest sutures in the iliopectineal ligament.

In those cases in which the fascia transversalis is attenuated, producing in effect a fascial gap in the floor, there have been proposed three methods of augmenting it: (1) By making a relief incision in the rectus sheath (Fig. 3), the components of the aponeurotic stratum may be displaced lateralward and overlie the subfunicular area of weakness, or the fascial sheath may be reflected and sutured to Cooper's ligament. The objection to the latter is that it predisposes to herniation by the creation of a spindle-shaped gap at the lateral border of the rectus muscle. (2) Another method is by weaving a living fascial suture between the medial fascial boundary and the iliopectineal ligament. In this way a permanent fascial barrier is formed spanning the vulnerable floor. (3) Perhaps the method that

is rapidly gaining favor is a combination of the relief incision of Fallis with a fascial suture.

The primary objectives of the second step of the combined operation are: obliteration of the interligamentous space and the stabilization, rarely the replacement, of the inguinal ligament. For the most part, it concerns the details in the placement of the second fascial suture in the alternate maneuvers depending on whether the interligamentous space is closed by a living suture or by turning down the lateral aponeurotic flap. Figures 5a and 6a show the second fascial suture passing through the loops of the first and through the inferior edge of the inguinal ligament beginning behind the pubic spine and continuing to the external iliac veins where it is reversed and returns attaching the edge of the lateral flap to the anterior surface of the medial. Figure 5b depicts the alternative technique in which the second suture passes through the loops of the first and through the turned down edge of the lateral flap. It continues in this manner to the external iliac vein or transitional level where it is reversed (Fig. 6b and 7b) passing through the adjacent anterior surfaces of the aponeurotic flaps. In both variants the cord is transposed extra-aponeurotically.

In those rare instances in which the inguinal ligament is totally absent, usually having been destroyed by trauma or infection following a previous repair, Wilmoth has constructed an inguinal ligament by raising a pedicled rectangular flap of the tensor fascia femoris muscle with its enveloping fasciae. The flap is swung into the inguen below the anterior-superior spine of the ilium. Its inferior edge is sutured to Cooper's ligament from the pubic spine to the iliofemoral vein. This unique variant of Wilmoth is worth remembering; but it has not been used in our experience.

CONCLUSIONS

1. Iliopectineal (Cooper's) ligament hernioplasty has been defined in the light of present progress, distinguishing it from the conventional inguinal ligament hernioplasty.

2. Factors responsible for the reluctance of surgeons to accept Cooper's ligament repairs have been discussed.

3. Absolute and equivocal criteria for the *combined operation* are given.

4. A classification of iliopectineal ligament hernioplasty has been presented from the point of view of evolution and correlation of the various technical maneuvers with the vulnerable area for which each variant was designed to correct.

5. A composite operation incorporating the different reparative departures of Cooper's ligament technique is submitted.

6. Often, because of one's enthusiasm there is a tendency to prejudge a technique before there is available adequate follow-up statistics. This should restrain our expectancy for any new or revived maneuver, no matter how valid it may seem at first. Fundamental principles, anatomical and surgical, still hold. The correlation of the weakness present with the knowledge of the available means for its repair remains paramount in the treatment of hernia.

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SUPERFICIAL LOBECTOMY AND TOTAL PAROTIDECTOMY WITH PRESERVATION OF THE FACIAL NERVE IN THE TREATMENT OF PAROTID TUMORS

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ALTHOUGH mixed tumors of the parotid gland are relatively infrequent (comprising about 4 per cent of all tumors of the oral cavity and adjacent region) (12) still the high incidence of recurrence following excision gives them added importance. The recurrence rates of between 20 to 40 per cent (5), are due mainly to inadequate excision of the neoplasm. The very fact that the tumor is usually poorly encapsulated and contains myxomatous tissue, is probably directly responsible for its incomplete removal when the surgeon attempts to enucleate the tumor from the surrounding parotid tissue. Inadequate excision is also encouraged by the fear of injury to the facial nerve. By the usual surgical approach, the facial nerve is not visualized and consequently its position in relation to the tumor is unknown. The results of injury to the seventh cranial nerve are so blatantly evident that one can readily appreciate the tendency for the surgeon to be most conservative in an effort to avoid this disaster.

Recurrences following surgery are of importance because they tend to grow rapidly and disseminate far into normal tissue. Further, about 25 per cent of mixed tumors (14) tend to become malignant following the appearance of recurrent growths.

ANATOMICAL CONSIDERATIONS

Anatomy textbooks (10) usually describe the seventh cranial nerve as running through the parotid gland. The careful dissections of McWhorter, however, showed that the facial nerve does not run through the parotid gland but rather it courses between the superficial and deep parts of this salivary gland. Our dissections on the cadaver substantiate McWhorter's findings.

The nerve has the same relationship to the two parts of parotid gland as a bookmarker has to two pages of a book that it separates. After emerging from the stylomastoid foramen the nerve passes anteriorly and laterally to the mastoid process and then comes to be deep to the superficial portion of the gland. The nerve is then split into two main divisions, the temporofacial and cervicofacial nerves by the isthmus connecting the deep and superficial portions of the parotid. These divisions in turn, divide and emerge at the anterior border of the parotid as five terminal branches (Fig. 1): the temporal, zygomatic, buccal, mandibular and cervical nerves.

McCormack, Cauldwell, and Anson have described in detail the variations of the terminal divisions of the seventh cranial nerve and the anastomosis connecting the cervicofacial and temporofacial divisions. Furthermore, they have confirmed the findings of McWhorter concerning the relationship of the facial nerve to the superficial and deep part of the gland.

The parotid has no true capsule. It is covered laterally by the parotidomasseteric fascia which is tough and dense posteriorly but becomes thin and fades at the anterior border of the gland. The gland lobules are held together by thin areolar tissue and this same type of connective tissue separates the medial surface of the superficial part of the gland from the facial nerve. The isthmus forming the superficial and deep portion of the parotid varies considerably in thickness; in fact, it may be entirely absent. The deep portion of the gland is wrapped about the external carotid artery and its two terminal branches, the internal maxillary and superficial temporal arteries. The posterior facial vein which is formed by the union of the superficial temporal and middle temporal veins passes down in the substance of the deep lobe of the parotid with the external carotid artery.

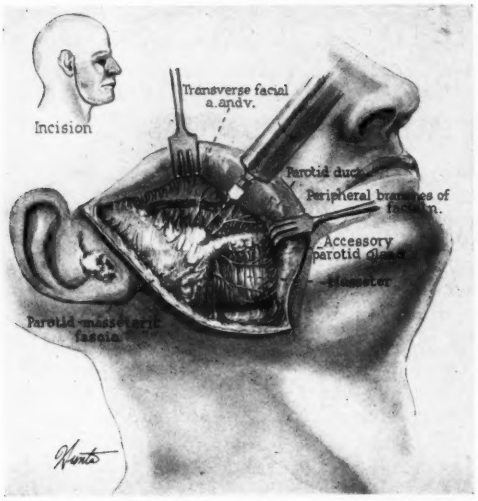

Fig. 1. Skin flap dissected to expose entire superficial lobe of parotid. Dissection in the plane between the facial nerve and gland is begun anteriorly. The injection of a few cubic centimeters of saline in the loose areolar tissue between the parotid and the nerve aids the dissection. Insert shows skin incision.

OPERATIVE TECHNIQUE

The anesthesia used is Baird's solution (pentothal-curare solution) with oxygen administered through the intratracheal tube (4). The incision (Fig. 1) extends vertically from the zygomatic process to a finger-breadth below the angle of the mandible and then forward to the posterior border of the submandibular gland. The vertical component of the incision passes through the natural longitudinal skin creases immediately in front of the external ear and hence is barely visible after it has healed. The horizontal component is similarly well hidden under the ramus of the mandible. The skin flap is then raised and dissected anteriorly until the anterior border of the parotid and the parotid duct are visible beneath the thin, fading parotidomasseteric fascia. This initial dissection of the skin flap must be done with meticulous hemostasis for the planes of dissection which must be obtained can readily be missed in a field which is being covered with blood from multiple small oozing points.

Beyond the medial (deep) to the exposed superficial portion of the parotid the terminal branches of the facial nerve are readily seen (Fig. 1). The parotid duct is next identified and transected. The distal end is tied with a No. 0000 suture and the proximal end is similarly treated, with forceps left attached so that gentle traction may be placed upon it. With any of the readily visible anterior terminal branches of the facial nerve as a landmark, blunt dissection is carried out gently and carefully by spreading with small curved mosquito forceps. The plane that must be entered is that between the medial (deep) surface of the superficial part of the parotid and the branches of the facial nerve. This plane is composed of loose areolar tissue and to facilitate its recognition gentle traction outward is put on the transected proximal end of the parotid duct. A few cubic centimeters of saline solution containing 6 drops of adrenalin to the ounce are also injected into this plane, so that an artificial separation is produced between the gland and nerve. The adrenalin causes local vasoconstriction and aids in effecting hemostasis. The dissection proceeds from the anterior border of the gland posteriorly until the level of the isthmus is reached (Fig. 2). Greatest difficulty is experienced in starting the dissection anteriorly and particularly about the parotid duct where almost invariably several small communicating nerve fibers are closely adherent to the lateral aspect of Stenson's duct. The fact that this dissection must be done carefully, gently, and without haste cannot be too strongly emphasized. When the isthmus is reached the site of bifurcation of the main trunk of the facial nerve can be readily visualized and thus avoided in the remainder of the dissection. The posterior border of the superficial portion of the parotid is next dissected from the external auditory canal and adjacent sternomastoid muscle. This portion of the dissection is vascular and must be carried out slowly and carefully. By carrying this dissection anteriorly the isthmus and the seventh cranial nerve is again reached. By transecting the isthmus the superficial portion of the gland is removed. The deep portion is removed (Fig. 3) by transecting the external carotid artery and posterior facial vein at the inferior border of the deep lobe, the superficial temporal artery and vein at the superior border and the inter-

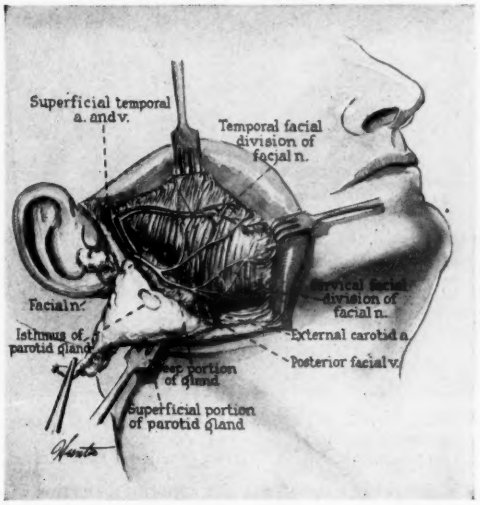
Superficial temporal a. and v.
Temporal facial division of facial n.
Facial n.
Isthmus of parotid gland
External carotid a.
Posterior facial v.
Superficial portion of parotid gland

Fig. 2. Superficial lobe of parotid dissected back to isthmus already transected. Note relationship between facial nerve and superficial and deep portions of parotid.

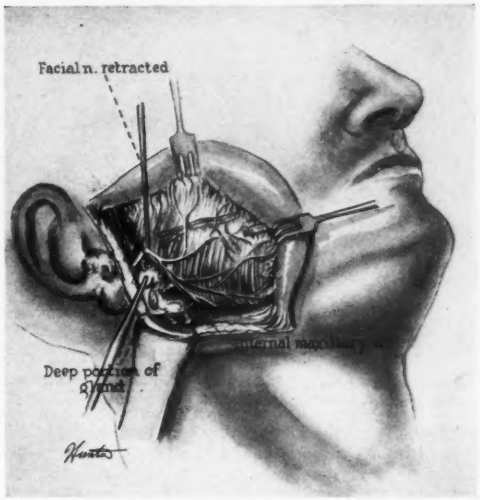

Fig. 3. Superficial portion of gland has been resected. The facial nerve is retracted and the deep portion of the parotid is removed.

nal maxillary artery at the mid-portion of the anterior border of the deep lobe. By elevating the facial nerve with a nerve hook the deep part may be dissected away from the main stem of the nerve and lifted out as a separate unit.

The operative site is checked carefully for bleeding points and after thorough irrigation with saline solution, the subcutaneous tissues of the incision are approximated with No. 000 plain catgut and the skin is closed with interrupted No. 0000 silk. A small Penrose drain is brought out through a small stab wound posterior to the incision in a dependent portion beneath the angle of the mandible. This is left for 48 hours only.

INDICATIONS FOR SUBTOTAL AND PARTIAL PAROTIDECTOMY

Because mixed tumors of the parotid are usually so poorly delineated from the surrounding gland tissues and because they may be multicentric in origin (1, 15) we believe that attempts at enucleation of the tumor will result in continued high recurrence rates. For these reasons we have decided to treat some of the patients with tumors of the superficial lobe of the parotid with superficial lobectomy, and in the remainder a total parotidectomy will be done. It is hoped by observing the recurrence rate in both groups that an answer will be available as to the best method of treating the superficial tumors.

Patients with tumors of the isthmus and deep portion of the gland should have total parotidectomies, similarly, if there is any suspicion as to the presence of malignant degeneration of the tumor, a total parotidectomy should be done.

CASE REPORTS

CASE 1. A. K., No. 736705, a white female, 56 years of age, was first seen in the outpatient tumor clinic at the University Hospital on October 28, 1946, complaining of two masses just behind the angle of the mandible on the left side, of 3 months' duration. These masses had grown steadily but slowly until they collected to form one and had caused patient intermittent moderately severe pain, particularly on opening and closing of the jaws. Examination revealed a mass about 2 by 3 centimeters just behind the angle of the left mandible, with an irregular firm surface and well defined nodular border. The tumor was moderately tender. There were no enlargements of the left cervical nodes and the chest plate was negative for metastases. The clinical impression was mixed tumor of the left parotid. On December 30,

Fig. 4, left. A. K., 3 months after left total parotidectomy.
Fig. 5. Same patient. Note intact junction of facial nerve.

1946, a left total parotidectomy was done. The exposed tumor was ill-defined and appeared to be multinodular. It would have been very difficult to enucleate the tumor because of its apparent multinodular character. The pathological examination revealed the superficial portion of the parotid to be almost completely replaced by multinodular tumor with the largest nodules measuring up to 1.5 centimeters. Microscopic sections revealed the tumor to be composed chiefly of epithelial cells arranged in cords separated by hyaline connective tissue. In one or two areas were gland-like structures containing a mucous material in the center. The pathological diagnosis was cylindromatous type of mixed tumor. Following operation there was a temporary paresis of the muscles about the mouth which lasted for about 2 weeks. This patient was last seen on February 26, 1948. Examination revealed no evidence of recurrence and complete return of the facial nerve function (Figs. 4, 5).

CASE 2. R. W., No. 776033, a white male, 35 years of age, was first seen at the University Hospitals, on February 26, 1947, complaining of a small mass beneath the right ear which had been present for about 25 years. During the 6 months prior to his hospital visit the tumor had increased in size, slowly but definitely, and in addition he noted pain down the right side of the neck. He also stated that he had noticed slight numbness of the right side of the face and slight asymmetry of the right corner of the mouth. Biopsy of the lesion by his doctor about 3 weeks prior to his admission to the University Hospitals resulted in a pathological report of mixed tumor of the parotid. Examination revealed a single mass, 3 by 4.5 centimeters, in retromandibular subauricular space with a recent biopsy scar over the prominence of the tumor. The facial nerve was intact and the remainder of the physical examination was essentially negative. On February 27, 1947, a right total parotidectomy was done. The skin overlying the mass was also removed. The pathological report revealed a single circumscribed mass 2 by 5

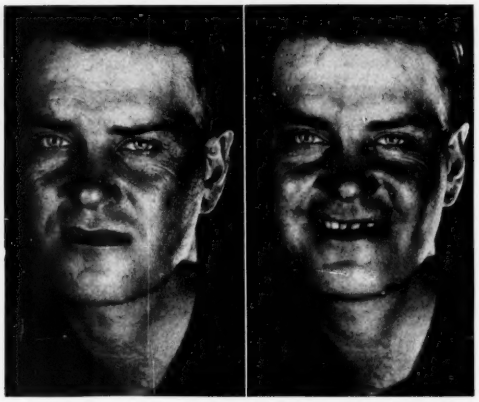

Fig. 6, left. R. W., 17 months following right total parotidectomy.
Fig. 7. Same patient. Note intact junction of facial nerve.

centimeters in diameter in the superficial portion of the gland. Microscopically the tumor was of a mixed type composed chiefly of myxomatous tissue divided into coarse rounded lobules by slender strands of connective tissue. Throughout there were scattered epithelial cords. After operation the patient had slight paresis of the orbiculus oculi muscle which lasted about 4 months. He was last seen on June 13, 1948, at which time there were no evidences of recurrence of the tumor, and the facial nerve function had returned completely (Fig. 6, 7).

In addition to these 2 cases,[1] 4 patients had superficial lobectomies and 5 have had total parotidectomies, and in all individuals except one, the seventh cranial nerve has been spared. In one case with recurrent tumors the cervical branch of the facial nerve was inadvertently transected. These cases have been done too recently to warrant any comments concerning recurrences.

DISCUSSION

Our own anatomical dissections of the parotid gland confirmed the observations of McWhorter and led to the adoption of the surgical technique described. McCormack, Cauldwell, and Anson also suggested from their dissections that parotidectomy could be done by starting at the anterior aspect of the gland. Sistrunk in 1921 and Adson and Ott in 1923 suggested the identification of the inframandibular branch of the facial nerve as the starting

[1]Since this paper was submitted for publication 11 additional patients have had superficial lobectomies and 9 have had total parotidectomies.

point for removal of the parotid gland without injury to the facial nerve. Like H. Bailey (2) we have found it has been difficult to identify this branch readily in all patients.

Hamilton Bailey (2, 3) has also been a strong advocate of adequate exposure of the parotid gland before an attempt to remove the tumor is undertaken. He begins his dissection of the superficial lobe of the parotid at the lower anterior border of the gland. The main trunk of the facial nerve is identified posteriorly with the digestive muscle as a guide. Janes advocates identification of the stem of the facial nerve soon after it leaves the stylomastoid foramen. However, the depth of the stylomastoid foramen makes this approach to the facial nerve more difficult than the one described in this paper, where identification of the nerve fibers is made where they are superficial.

Parotidectomy performed by the technique described above is admirably suited for dealing with mixed tumors of the parotid. There is no question of trying to determine the extent of the tumor, of violating the pseudocapsule, and of injury to the facial nerve. Further, if there are multiple small tumors, as was present in one of the cases reported, or if there is a possibility of multiple foci of origin of mixed tumor as suggested by Ewing, total parotidectomy should result in a marked decrease in recurrent growths following surgery. The validity of this contention can be established only with the passage of time, for as McFarland pointed out, the average interval before recurrence after surgery was approximately 7 years, although a goodly number of recurrences appeared within a year of surgery.

By defining the anterior border of the gland, then dissecting posteriorly between it and the facial nerve the only part of the gland substance that is entered is the thin isthmus. This technique is used to facilitate the dissection. However, if the tumor occupies the isthmus, the transection of this part of the parotid is avoided and the whole gland is removed intact. This technique results in more handling and trauma to the facial nerve with a consequent longer period before recovery of its functions occurs.

Radical excision of the superficial portion of a parotid or a total parotidectomy should be considered for all solid tumors of the gland, for these neoplasms should be assumed to be malignant until proved otherwise. On reviewing pathological section of 210 parotid tumors at the Mayo Clinic, Quattlebaum and coworkers found 21 instances in which a previous diagnosis of a typical mixed tumor was reversed to adenocarcinoma of the cylindroma.

SUMMARY

1. The high recurrence rate following excision of parotid tumors is due primarily to inadequate excision of the tumor.

2. The lack of a true capsule and the myxomatous type of tissue of the tumor makes it difficult to determine the true extent of the neoplasm.

3. Fear of injury to the facial nerve also makes for inadequate conservative excision of parotid tumors.

4. The possibility that parotid tumors may be multiple or arise from multiple foci in different portions of the gland is also suggested as a possible cause of the high recurrence rate.

5. Radical excision of solid parotid tumors is also recommended because they may be malignant.

6. A surgical technique of superficial lobectomy of the parotid and total parotidectomy without injury to the seventh nerve is described.

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AUGUST, 1949

THE TREATMENT OF CARCINOMA OF THE VULVA

CARCINOMA of the vulva is not a clinical entity. At some unknown time long ago the custom was established of including under this term carcinoma of the glans clitoris, of Bartholin's gland, some other glandular tumors and, occasionally, melanosarcoma of the vulva, along with the more common epithelioma of the labia, adjacent perineum, and vestibule. These represent such a variety of lesions from almost all points of view that there would seem to be no justification for grouping them together. There are however, two reasons for continuing the tradition. Therapy has been similar throughout the group though yielding different degrees of effectiveness. The common epithelioma makes up an overwhelmingly large proportion of the total tumors so that inclusion of the special tumors has not seriously interfered with the expression of results. They may then be considered as a group in the present discussion of treatment.

Carcinoma of the vulva has been a relatively rare disease. But since it is characteristically a disease of advanced age, an increasing number may be expected as the age of the population increases. In general, use is not being made of knowledge and experience, the application of which has been demonstrated to improve very significantly the end results. For these reasons, it would seem wise to try to reach an understanding as to the problems, the attack, and the rewards in this condition. The object of this discussion is to demonstrate the applicability, effectiveness and safety of single stage radical vulvectomy under local anesthesia and to urge the acceptance of it as the standard method of treatment.

An astonishing variety of combinations of treatment forms has been applied to vulva carcinoma. At the University of Minnesota from 1928 through 1938, there were approximately half as many such combinations used as there were patients treated. This yielded a five year cure rate of 15 per cent. No single stage radical vulvectomy was done during this time but all manner of combinations of simple vulvectomy, gland resection, x-ray, surface and interstitial radium were used. Such excessive individualization of therapy can mean only that none of it was satisfactory, and the result produced would seem to confirm this. Anyone who has studied such clinical material will have little difficulty in arriving at the conclusion that simple vulvectomy is not an effective method of treatment. Irradiation is not even useful as a palliative procedure. Adequate depth doses cannot be obtained without destroying the skin of this sensitive area. And the tumor is radioresistant. While no standard arrangement of the two stage combina-

tion of vulvectomy and bilateral gland resection was applied in this material, the combination as it was carried out was not sufficiently effective to recommend it.

One gets the impression that three attitudes have brought about the decision to undertake minor forms of treatment. Many of the patients are old and there is a very natural fear of the surgical risk involved. The poor results of minor therapy in these have been observed and the conclusion drawn that the disease is relatively incurable. And finally, too much importance has been ascribed to the problem of obtaining primary healing of the wound in the more extensive dissection of the single stage procedure.

On the other hand, the single stage radical removal of the vulva together with the inguinal and femoral glands in one intact piece has many attractions. It satisfies the generally applicable basic principles of surgical attack on malignant disease. Dissection is carried out in healthy tissue without cutting into the tumor or its lymph drainage area. This latter is removed intact to a point beyond which extension of the surgery will add more to the mortality of the procedure than it will to the cure rate. Bilateral gland removal is always done since it has proved impossible to determine accurately by clinical examination the presence or absence of gland metastasis, and since contralateral metastasis is frequent. The poor results shown to follow lesser procedures recommend the radical approach.

And now let us see what can be done with this radical approach. If it is to be useful, it must have a wide applicability, be reasonably free of serious after effects, produce a real increase in the cure rate and have a reasonably small primary procedural mortality. Ten years ago the department of obstetrics and gynecology at the University of Minnesota Medical School set out to study these problems. Only single stage radical vulvectomy under local procaine and adrenalin anesthesia was used in treatment. Except for minor variations in technique, this has not been changed during the period of study. The results have been reported in detail elsewhere. Every patient was included, whether she had been previously treated or not. Many had practically hopeless recurrences when first seen. A number had been refused treatment as hopeless by competent gynecologists. Some of the five year cures were derived from this latter group.

In more than 90 per cent of the patients, single stage radical vulvectomy was carried out. Four were not so treated because of extensive metastases above the inguinal and femoral gland groups. One refused treatment and one had no demonstrable tumor on biopsy or on examination of the simple vulvectomy specimen by two departments. It was found later as a microscopic tumor when the specimen was being completely cut for other purposes. No patient was excluded from surgery because of the local extent of the tumor or because of other physical abnormality. The applicability of the procedure is then practically complete where any reasonable hope of recovery exists. One is satisfied that the largest single factor in this degree of applicability lies in the use of local anesthesia.

No serious after effects have been seen. Occasionally edema of one or both legs may be present, particularly in obese women, for some time after operation. This has never been more than a nuisance. The local scar has not produced trouble.

More than 50 per cent of these patients were alive and free of tumor after five years. In view of the fact that a large proportion of these patients had advanced or recurrent tumor and many were very elderly, this cure rate would lead to the conclusion that carcinoma of the vulva ranks among the best of the

human cancers in its response to adequate therapy. Indeed, given a patient with a reasonable life expectancy and a reasonably early tumor which has not been tampered with, radical vulvectomy offers an excellent probability of permanent cure.

What operative mortality price was paid for this? Six per cent of the patients operated upon died before discharge from the hospital. None of these died in immediate association with the surgical event. One very old lady simply faded away some weeks after surgery and even autopsy failed to show a definite cause. One, who had a complete heart block before operation eventually died of this. One with a known preoperative pyelonephritis underwent a flare-up of this and died as a result. Two deaths were caused by pulmonary emboli. This does not seem to be too great a price to pay for the results achieved.[1]

It would seem fair to conclude that single stage radical vulvectomy under local anesthesia routinely applied as early as possible but irrespective of the earliness or lateness of the local tumor and almost irrespective of the age or general physical status of the patient, offers the opportunity of reasonably safely increasing by three to five fold the salvage rate of lesser procedures sometimes used in the treatment of carcinoma of the vulva.

JOHN L. MCKELVEY.

STREPTOMYCIN IN SKELETAL TUBERCULOSIS

As clinical data accumulate, it is evident that streptomycin and its derivatives are really effective weapons for use in the treatment of tuberculosis of the bones and their allied structures. Tuberculosis, a slow unrelenting process, must be observed for prolonged periods in order to determine its progression or arrest. This is especially true of tuberculosis in and about bones; therefore, these observations are being made with caution on tuberculosis of bones and joints.

It has been pointed out many times that when a therapeutic agent is carried to its desired destination by the blood stream, it does its best work if this region is flushed with blood. To date the best results from use of streptomycin in the treatment of tuberculosis of bones and allied structures have been in early tuberculosis of the soft tissues and synovia before bony involvement or soft tissue fibrosis has developed. At this time, frequently, the diagnosis is in doubt, but it should be proved by biopsy, culture, and animal inoculation. In several proved cases of synovial tuberculosis, a second biopsy after a course of streptomycin therapy has been negative for tuberculosis. The clinical results have been just as dramatic and what appears to be a cure has been effected. Fulminating open lesions of the extremities have been seen to return to a nearly normal status after a course of treatment with streptomycin. In the past many tuberculous sinuses and bursae were excised and cured without streptomycin, but with streptomycin as an adjunct complete and thorough excision of these lesions now can be done with greater assurance of healing.

Tuberculous lesions of the shafts of long bones are sufficiently rare, so that, as far as I know, no experience has been gained in their treatment with streptomycin.

The treatment of tuberculosis of joints presents two distinct problems. In a weight-bearing joint where the demand is for a nearly normal structure which can maintain its function without mechanical flaws, the problem is more difficult than in a nonweight-bearing joint where the demand on the joint is not so exacting. In the weight-bearing joints it

[1]For further details reference is made to the *American Journal of Obstetrics and Gynecology*, 1947, 54: 626 and to the multiple reports of Taussig.

especially is important, then, to make an early diagnosis and institute treatment while the infection is still limited to the synovia and cartilaginous margins of the joint. When the diagnosis is made this early, these joints have been and can be salvaged and their function retained. There are decided opinions as to whether joints of this sort should be immobilized during treatment. Traditionally, rest is indicated for the cure of tuberculosis. Practically more hyperemia and active dispersal of the streptomycin throughout the joint and its adjacent structures may occur when active motion without weight bearing is allowed. In cases which I have observed personally, the joint has been less stiff after treatment is stopped if it is allowed to be mobile during treatment. Obviously, streptomycin can be considered only an adjunct to surgical treatment when the articular surfaces are sufficiently destroyed so that even if the tuberculosis were arrested, traumatic arthritis would be present. It seems to me, however, that a preoperative course of treatment with streptomycin has allowed excision and arthrodesis in cases of fulminating tuberculosis of the joints in which the chances of success without it were slight. In the past amputation would have been necessary in many of these cases. Treatment with streptomycin also seems to have lessened the danger of disseminated tuberculosis and persistent draining sinuses and mixed infections do not appear to be as common before operation as formerly.

In lesions of the nonweight-bearing joints, it does not appear that arthrodesis will need to be recommended as frequently as it was when streptomycin was not available. This statement is made with some reservations because, in cases of extensive fibrotic and sclerotic tuberculosis about these joints, a period of arrest followed by reactivation in a year or two has been noted. This reactivation may or may not be controlled by a second course of streptomycin. The danger of appearance of strains of tubercle bacilli resistant to streptomycin has to be considered in these cases. Experience is not great enough, as yet, for anyone to know whether streptomycin should be considered an adjunct to surgery or as a complete therapeutic agent for tuberculosis of these joints. It is possible that, at present, with the more conservative attitude, we are missing the golden opportunity to succeed with arthrodesis. We will have to await the lesson of experience.

Solutions of streptomycin have been injected into the joints but the drug appears to be somewhat irritating. Clinical experience has shown, however, that effective concentrations can be obtained within the joint by intramuscular injection.

Tuberculosis of the spinal column presents a somewhat more difficult problem of analysis. Even when roentgenograms are good, critical evaluation of destruction and repair can vary within broad bounds. Conclusions on results must be slowly formed because of the nature of the disease and the nature of bone repair itself. Thus far, preliminary surveys are mildly favorable. If the disease is fairly advanced and was discovered late, too startling a result cannot be expected. The disease is serious enough so that all modes of treatment, including streptomycin, are being used. Rest and spinal fusion in the past effected cures so that everyone concerned must be cautious about giving too much credit to streptomycin. I believe, however, that it facilitates the process of healing.

The exact place of streptomycin in the treatment of tuberculosis of bones and allied structures is not known as yet. At the end of the next decade of study its place should be evaluated better than at present.

WILLIAM H. BICKEL.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE fourth book in the series *British Surgical Practice*[1] begins with the subject of "Facial Palsy" and ends with "Hiccup."

The editors have adhered closely to their original promise to select authorities in each field and to permit each author to develop his topic without interference. Subjects are listed in alphabetic order entirely, so there is no central theme for any one volume. Concise review of the entire volume is therefore impossible, but certain features are outstanding and deserve comment.

Many of the topics in the present volume might be considered decidedly nonsurgical in scope, for example, filariasis, frostbite, gonorrhea, gout, and herpes zoster; and the casual observer might feel that for the sake of brevity many of these could be omitted. However, the set of volumes includes at least brief references to many situations which will confront the doctor, especially one who is in a remote community. The delightful style apparent in the first 3 volumes is still a feature and makes pleasant reading.

The discussion of facial palsy emphasizes injuries to nerves likely to occur in performing radical mastoidectomy. The illustrations are excellent; the outline method of presentation is convenient; and the general discussion is adequate. The enthusiasm of the author of this section for various procedures leads the reader to feel that operations, such as nerve crossing and anastomosis, are attended by far happier results than certain American authorities have achieved.

The chapter on maxillofacial injury is clear and concise. Most of the present knowledge on this subject is included, although the references are a bit brief. It is interesting to note that in the discussion of treatment of fracture of the jaw space is devoted to the use of multiple pins for external fixation. It seems somewhat surprising that there is so little mention of war injuries. Complications and postoperative care could well have received more detailed discussion.

A fascinating chapter on fascial grafts by no less an authority than Professor Gallie presents the background for use of fascia as a living or nonliving suture, and there are excellent illustrations of the proper application of the suture. The convenience of the Masson stripper is emphasized. The reviewer realizes that the use of fascial grafts may become a lost art if the young surgeon of today does not master the technique required for successful use of this valuable aid because so many foreign substances, such as wire, screen, and mesh gauze, are now being used to supplant fascial grafts. Professor Gallie's chapter is most timely in that regard.

The miscellaneous chapters on fields of greater or lesser surgical interest will probably be of use to a limited group of surgeons. A long and complete outline on surgery of the foot is outstanding, and the diagrams and illustrations are very practical; they will probably be used widely as an authoritative reference for the busy practitioner. Other chapters deal with orthopedic problems including those of the upper extremity, clavicle, femur and some of the smaller bones. It is noteworthy that considerable space is devoted to the use of appliances and splints, and relatively little comment is directed toward open operation with internal fixation which is used extensively in many centers today.

One of the most valuable chapters is the one dealing with the gall bladder and bile passages. A convenient outline presents briefly the historical background where indicated and, at the same time, brings the reader up to date on many of the newer concepts. The portion dealing with acute cholecystitis is in complete accord with leading surgical thought in America. Warnings are sounded at the proper places and pitfalls and safeguards are stressed properly. Each feature is catalogued in alphabetic sequence and, although brevity is the keynote of the chapter, completeness is one of its strong points. The American surgeon will note with interest the discussion on acquired stricture of the common bile duct. Recently, American specialists in internal medicine have tended to point to Great Britain because it seemed that tragedy of this type was almost unheard of there. However, British surgeons apparently still do encounter an occasional case and have just as much difficulty with this problem as American surgeons have. It is noteworthy that the author predicted a brilliant future for those patients who had undergone reconstruction of the common bile duct over vitallium tubes. It may not be common knowledge but the fact remains that the use of vitallium tubes has been met with almost universal failure because they become plugged. Little is included concerning the Whipple operation and its modifications. The assumption is that a subsequent volume will contain more discussion of malignant lesions in the biliary system.

[1] BRITISH SURGICAL PRACTICE. Under the general editorship of Sir Ernest Rock Carling, F.R.C.S., F.R.C.P., and J. Patterson Ross, M.S., F.R.C.S. Vol. 4. London: Butterworth & Co., Ltd.; St. Louis: The C. V. Mosby Co., 1948.

The chapter on gas gangrene follows a logical sequence; namely, a comparison of the experiences in World War I with those in World War II. It is of interest that the author felt that penicillin might change the entire picture of this dread complication. The consensus now is that penicillin has been of little or no value in the treatment of patients who have gas gangrene; at least this proved to be true in the series of cases observed in the American army in the Pacific area.

One reads with mixed opinions the chapter on gland puncture and aspiration biopsy. This seems to be a controversial topic throughout the civilized world today. Although most of the points that the author makes are undoubtedly true and the illustrations he presents are excellent, many American authorities hold this technique in a questionable light. They feel that for biopsy removal of actual tissue with the scalpel is a thorough and less dangerous method. Many surgeons in America endeavor to supply the pathologist with an adequate amount of tissue for a final opinion and feel that this method is more satisfactory than obtaining the specimen for biopsy with the needle. In the United States there has been an evolution from obtaining a specimen of the liver for biopsy by needle. Two years ago the great enthusiasm for this method led to the inevitable situation: hemorrhage was encountered which required laparotomy for control. In scattered reports it has now been learned that in a few cases this type of biopsy has resulted in death of the patient.

Some miscellaneous topics are of considerable interest if only because of the knowledge that the data are available for ready reference in this volume. The chapters concerning gunshot wounds are rather too brief, inasmuch as the average reader of these volumes will undoubtedly be in a position to require considerable information on the proper management in this type of case. Strangely enough, more space is devoted to reconstructive surgery than to acute injuries. The same criticism might apply to this volume which was offered in previous volumes; namely, that patients requiring reconstructive surgery might profit greatly if they were referred to special centers where proper definitive treatment could be carried out.

The detailed discussion of hernias is indeed timely, as the tremendous advances in surgery might lead the young surgeon to overlook this type of lesion. Thorough understanding of the primary situation should reduce the necessity for much experience with recurrent hernias. This part of this volume is one of the most valuable of all.

The volume ends with a short chapter on hiccup. Evidently this is as much of a problem in the British Isles as it is in the United States and the variety of methods used in attempts to overcome this distressing condition is testimony to the obvious fact that there is no reliable method. Brief comment is made about interruption of the phrenic nerve with the conclusion that "this can rarely be justified."

E. S. JUDD, JR.

THE fourth edition of the *Manual of Urology*[1] by Ralph M. LeComte is a valuable contribution to the field of urologic literature.

The author has tried to write for the student beginning the study of urology. This aim has been achieved, and the simplicity of the text is one of its most outstanding features. It should be in the hands of every senior medical student.

That portion of the text dealing with infections of the urinary tract is as up to date as it can possibly be. The material on chemotherapeutic agents and antibiotics is authoritative and is clearly written.

It is of interest to notice how the author handles such controversial material as nephroptosis and ureteral stricture. His words are certainly conservative.

He believes that all diagnostic procedures and all other therapeutic procedures should be carried out carefully before considering nephropexy. Likewise, he feels that, while a ureteral stricture certainly may occur, its frequency is not as great as formerly believed, and the symptoms it causes are not as legion as previously considered.

One of the best sections in the book is that concerning the treatment of benign prostatic enlargement. The author considers all sides of this problem and then gives his own opinion. He favors open operation except in cases of small enlargement and cases of fibrosis of the vesical neck. In these cases, he believes that transurethral resection definitely is indicated.

The chapter on impotence and sterility in the male should be read by all practicing urologists and should benefit the general practitioner as well.

THOMAS L. POOL.

IN the volume *Principi di chirurgia del cervello e del midollo spinale*[2] (Principles of Surgery of the Brain and Spinal Cord), Africo Serra deals mostly with the surgical technique devised by Cushing, de Martel, Fedor Krause, Olivecrona, Elsberg, Frazier and their predecessors. Few of the recent advances are described or even mentioned in this book. The most important chapters deal with the subtemporal and suboccipital decompressions, the puncture of the corpus callosum for decompressive purposes, the frontal, frontoparietal and parieto-occipital craniotomies for the removal of tumors or the cure of jacksonian epilepsy, the different types of craniotomies of the posterior fossa, the temporal craniotomy for the relief of trigeminal neuralgia and the laminectomies. In 2 long, and perhaps the most interesting chapters, the author discusses the postoperative courses of the various types of brain tumors and their complications. He pays a great deal of attention to the influence of cerebral edema. The action of disturbances of the mesencephalic medullary centers on the centers of respiration, blood circulation, and

[1] MANUAL OF UROLOGY. By R. M. Le Comte, M.D., F.A.C.S. 4th ed. Baltimore: The Williams & Wilkins Co., 1948.

[2] PRINCIPI DI CHIRURGIA DEL CERVELLO E DEL MIDOLLO SPINALE. By Africo Serra. Bologna: Licinio Cappelli, 1948.

heart is illustrated by interesting case reports and is discussed from anatomical points of view.

Shorter chapters deal with interventions on the lateral and the third ventricles; however, the widely used Torkildsen procedure is completely ignored. The treatment of spastic torticollis is the one devised by Dandy and Olivecrona. The surgery of intracranial aneurysms is only briefly mentioned and the author states that he had only one such case. He also fails to mention the treatment of brain abscess, intracranial and intracerebral hematoma, hydrocephalus, platybasia, etc. He does not discuss any diagnostic studies, or the management of craniocerebral injuries.

The great value of the book lies mostly in the beautiful illustrations and especially the excellent colored drawings of operative fields and anatomical dissections made by the author himself. It also contains a large number of operative photographs showing the major steps in the various types of craniotomies. This 569 page book contains 401 text illustrations and 52 plates. GEORGE PERRET.

THE author of *Bronchogenic Carcinoma and Adenoma*[1], B. M. Fried, has drawn on the extensive experience of the Division of Chest Diseases of the Montefiore Hospital in New York and on the surgical literature in preparing this monograph.

[1]BRONCHIOGENIC CARCINOMA AND ADENOMA WITH A CHAPTER ON MEDIASTINAL TUMORS. By B. M. Fried, M.D. Baltimore: The Williams & Wilkins Co., 1948.

The chapters on the medical aspects of carcinoma of the bronchus are adequate and are profusely illustrated with pictures of gross specimens, photomicrographs, and reproductions of roentgenograms of the chest. In contrast, the treatment of the condition is covered inadequately, only 3 pages being devoted to the discussion of the surgical treatment. The same criticism might be applied to the chapter on adenoma of the bronchus, the treatment of which is discussed briefly in one-half page.

The questions of alveolar cell carcinoma and adenomatosis of the lungs are discussed together in a special supplement although there is no evidence that there is any relation between them. The author takes the dogmatic stand that alveolar cell carcinoma does not occur, attributing the condition to canalicular metastases from an invisible or overlooked carcinoma of the bronchus.

There is a lengthy discussion of the coincidental occurrence of carcinoma of the bronchus and pulmonary tuberculosis in the same patient. Another chapter is devoted to hypertrophic pulmonary osteoarthropathy which the author suggests is due to a "disturbance in the function of the organs of internal secretion." There is a final chapter on mediastinal tumors but this is incomplete and is of questionable value in this book.

Although the book is a worthwhile addition to the literature on carcinoma of the bronchus it does not satisfy the need for a complete review of our present knowledge about the condition. DAVID CARR.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

TEXTBOOK OF HISTOLOGY. By Jose F. Nonidez, D.Sc., and William F. Windle, Ph.D., Sc.D. 1st ed. New York, Toronto, and London: McGraw-Hill Book Co., Inc., 1949.

ARTHRITIS AND ALLIED CONDITIONS. By the late Bernard I. Comroe, M.D. Edited by Joseph L. Hollander, M.D., and collaborators. 4th rev. ed. Philadelphia: Lea & Febiger, 1949.

PSYCHOSOMATIC MEDICINE; THE CLINICAL APPLICATION OF PSYCHOPATHOLOGY TO GENERAL MEDICAL PROBLEMS. By Edward Weiss, M.D., and O. Spurgeon English, M.D. 2d ed. Philadelphia: W. B. Saunders Co., 1949.

ARMY FOOT SURVEY; AN INVESTIGATION OF FOOT AILMENTS IN CANADIAN SOLDIERS. By Colonel R. I. Harris, M.C., R.C.A.M.C., and Major J. Beath, R.C.A.M.C. Vol. 1, Main Report. Ottawa: National Research Council of Canada, 1947.

THE PREMATURE INFANT; MEDICAL AND NURSING CARE. By Julius H. Hess, M.D., and Evelyn C. Lundeen, R.N. 2d ed. Philadelphia, London, and Montreal: J. B. Lippincott Co., 1949.

MEDICINE OF THE YEAR. By Hugh J. Morgan, M.D., Frank Whitacre, M.D., Henry G. Poncher, M.D., and Warren H. Cole, M.D. Under the editorial direction of John B. Youmans, M.D. Philadelphia, London, and Montreal: J. B. Lippincott Co., 1949.

DIE INDIVIDUELLE REAKTIONSWEISE BEI CHIRURGISCHEN INFEKTIONSPROZESSEN. By Dr. Gerd Hegemann. Berlin, Gottingen, and Heidelberg: Springer-Verlag, 1949.

ANNALS OF ROENTGENOLOGY; A SERIES OF MONOGRAPHIC ATLASES. Vol. 17—ROENTGEN DIAGNOSIS OF THE EXTREMITIES AND SPINE. 2d enl. rev. ed. By Albert B. Ferguson, M.D. New York: Paul B. Hoeber, Inc., 1949.

DEMONSTRATIONS OF PHYSICAL SIGNS IN CLINICAL SURGERY. By Hamilton Bailey, F.R.C.S.(Eng.), F.A.C.S., F.I.C.S., F.R.S.E. 11th ed. Baltimore: The Williams & Wilkins Co., 1949.

REGIONAL ILEITIS. By Burrill B. Crohn, M.D. New York: Grune & Stratton, 1949.

EXPERIMENTAL SURGERY; INCLUDING SURGICAL PHYSIOLOGY. By J. Markowitz, M.B.E. 2d ed. Baltimore: The Williams & Wilkins Co., 1949.

MEDICAL ETYMOLOGY; THE HISTORY AND DERIVATION OF MEDICAL TERMS FOR STUDENTS OF MEDICINE, DENTISTRY, and NURSING. By O. H. Perry Pepper, M.D. Philadelphia, London: W. B. Saunders Co., 1949.

OPERATIVE TECHNIC IN GENERAL SURGERY. Edited by Warren H. Cole, M.D., F.A.C.S. Introduction by Frank H. Lahey, M.D., F.A.C.S. New York: Appleton-Century-Crofts, Inc., 1949.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

DALLAS B. PHEMISTER, Chicago, *President*
FREDERICK A. COLLER, Ann Arbor, *President-Elect*

PRELIMINARY PROGRAM FOR THE 35th CLINICAL CONGRESS—THE STEVENS, CHICAGO OCTOBER 17 TO 21, 1949

ALWAYS an outstanding international event, the Clinical Congress of the American College of Surgeons will in 1949 be exceptionally world-wide in representation because it will include the Sixth Inter-American Congress of Surgery and because many delegates from the thirteenth Congress of the International Society of Surgery which meets in New Orleans the previous week are planning to attend the Chicago Congresses. The Sixth Inter-American Congress of Surgery will actually be a seven-day meeting, extending from October 17 through 23, since it is meeting concurrently with the Clinical Congress of the American College of Surgeons and will continue in session two days after its close. Headquarters for both meetings will be at The Stevens.

Through the membership of the American College of Surgeons in the Association of Inter-American Congresses of Surgery, every Fellow is a member of the latter group and is entitled to attend its scientific and social sessions on Saturday and Sunday. The members of the signatory societies of the Association are likewise entitled to attend the Clinical Congress clinics and sessions. These facts should be borne in mind in making hotel reservations. The Inter-American Congress offers an excellent opportunity to enhance the international prestige of the American College of Surgeons, as well as to familiarize North American Fellows and overseas guests with surgical progress in the other Americas.

Preliminary plans for the Sixth Inter-American Congress of Surgery are described in a separate article which follows. It will be noted that the inaugural session, open to delegates only, will be held on Friday morning, October 21. The scientific sessions on Saturday and Sunday, and the official banquet on Saturday evening, are open to all Fellows, whose presence will help to demonstrate how deeply interested the American College of Surgeons is in the cultivation of mutually beneficial professional and social relationships among surgeons throughout the Americas.

PRELIMINARY PROGRAM

A varied and comprehensive program of meetings will be held at the headquarters hotel. A general assembly for both surgeons and hospital personnel will be the opening session on Monday morning, October 17. Scientific sessions, official meetings, hospital conferences, showings of medical motion pictures, and telecasts will follow during the five days of the Clinical Congress. The special sessions of the Sixth Inter-American Congress of Surgery on Friday, Saturday, and Sunday, will, according to present plans, be held in the John B. Murphy Auditorium of the College. All registrants for both Congresses will be interested in the extensive display of technical and scientific exhibits in the exhibition hall.

CLINICS

Operative and nonoperative clinics will be held in some twenty hospitals in the Chicago area each day during the Clinical Congress. The hospitals which will participate in the clinical program, and which are listed later in this article, are approved by the American College of Surgeons for graduate training in surgery. The schedule of clinics, which will cover general surgery, obstetrics and gynecology, fractures and other traumas, orthopedic surgery, thoracic surgery, plastic surgery, neurosurgery, genitourinary surgery, and ophthalmology and otorhinolaryngology, will be published in a *Daily Clinical Bulletin* which will be issued each day during the Clinical Congress. The clinic schedules will also be posted on bulletin boards.

TELEVISION

Operations will be telecast, in color, to the hotel from St. Luke's Hospital at scheduled periods each day. The television program will be over a closed circuit, impossible to pick up on public sets. The operations and demonstrations will be transmitted to about twenty color transmission receivers in the hotel. The engineers anticipate excellent reception since the hospital is in a direct line of vision from the roof of The Stevens. The television will be sponsored by Smith, Kline & French Laboratories.

The successful demonstrations of television at the Clinical Congress in New York in 1947, and at the Clinical Congress in Los Angeles in 1948, make it highly desirable to continue the use of this medium. Even when limited to black and white images, as it was then, the surgeons were most enthusiastic.

Television has proved to be an ideal means of furthering the "Show me" purpose which was the main incentive for the founding of the Clinical Congress of Surgeons of North America in 1910, three years before the American College of Surgeons was organized. That first Clinical Congress was held in Chicago. The 1949 meeting will be the ninth held in that city.

PRESIDENTIAL MEETING

The Presidential Meeting will be held on Monday evening, October 17. At this meeting the officers-elect, consisting of Dr. Frederick A. Coller of Ann Arbor, president, Dr. Donald G. Tollefson of Los Angeles, first vice-president, and Dr. Robert M. Moore of Galveston, second vice-president, will be installed. The outgoing president, Dr. Dallas B. Phemister of Chicago, will preside and will deliver the Presidential Address. His subject will be "An Evaluation of Fulltime and Group Practice for the Clinical Faculty of a Medical School."

Sir James R. Learmonth of Edinburgh will deliver the fourth Martin Memorial Lecture. His subject will be "Collateral Circulations, Natural and Artificial."

CONVOCATION

The formal initiation ceremonies for the new Fellows will be a colorful feature of the annual Convocation which will be held on the final evening, Friday, October 21. Honorary fellowships will also be conferred on this occasion. Lord Webb-Johnson of London, president of the Royal College of Surgeons of England, will deliver the Fellowship Address. His subject will be "Science in Surgery. Stop, and Look, and Listen."

EVENING SCIENTIFIC SESSIONS—GENERAL SURGERY

The program and speakers for the Tuesday evening general surgery session will be as follows:

Symposium—Acute Surgical Emergencies in Gynecology and Obstetrics:
- General Introduction. NEWELL W. PHILPOTT, M.D., F.A.C.S., Montreal.
- Tubal Pregnancy, Its Diagnosis and Treatment. LEWIS C. SCHEFFEY, M.D., Philadelphia.
- Pelvic Peritonitis Occurring in the Obstetrical or Gynecological Patient. FRANK GLENN, M.D., F.A.C.S., New York
- Emergency Cesarean Section. WILLIAM E. STUDDIFORD, M.D., F.A.C.S., New York.

The program and speakers for the Wednesday evening general surgery session will be as follows:

Fracture Oration. Fracture Hazards. OTTO J. HERMANN, M.D., F.A.C.S., Boston

Symposium—Blood Coagulation and the use of Anticoagulants:
- The Significance of Different Methods for Prothrombin Estimation and their Relative Values. JOHN H. OLWIN, M.D., Chicago.
- Studies on Antithrombin and Etiologic Factors in Phlebothrombosis. JOHN H. KAY, M.D., New Orleans.
- A Further Report on Dicumarol Prophylaxis against Venous Thrombosis in Women Undergoing Surgery. GEORGE VAN S. SMITH, M.D., F.A.C.S., Brookline, Massachusetts.

The program and speakers for the Thursday evening general surgery session will be as follows:

Symposium—Malignant Disease:
- Chemotherapy in Malignant Neoplastic Disease. CARL V. MOORE, M.D., St. Louis.
- Hormone Therapy of Cancer. CHARLES B. HUGGINS, M.D., Chicago.
- The Use of Radioactive Iodine in Studying the Pathologic Physiology of Thyroid Cancer. RULON W. RAWSON, M.D., New York.
- What We have Learned from Isotopes Concerning Depletion and Repair in Surgical Patients. FRANCIS D. MOORE, M.D., F.A.C.S., Boston.

GENERAL SURGERY PANEL DISCUSSIONS

General surgery panel discussions will be held on Monday, Tuesday, and Wednesday afternoons, from 1:30 to 3:00 and from 3:30 to 5:00 o'clock. The subjects and the names of the moderators follow:

Monday—1:30 to 3:00 p.m.

Surgical Lesions of the Breast. GEORGE G. FINNEY, M.D., F.A.C.S., Baltimore.

3:30 to 5:00 p.m.

Fractures of the Skull. ELDRIDGE H. CAMPBELL, M.D., F.A.C.S., Albany.

Tuesday—1:30 to 3:00 p.m.

Massive Upper Abdominal Hemorrhage. JOHN H. MULHOLLAND, M.D., F.A.C.S., New York.

3:30 to 5:00 p.m.

New Surgical Techniques in Drug Treated Infections. CHAMP LYONS, M.D., New Orleans.

Wednesday—1:30 to 3:00 p.m.

The Management of Acute Emergencies Occurring During Operations. I. MIMS GAGE, M.D., F.A.C.S., New Orleans.

3:30 to 5:00 p.m.

Preoperative and Postoperative Care and Anesthesia for Infants. THOMAS H. LANMAN, M.D., F.A.C.S., Boston.

SPECIAL FIELDS OF SURGERY

Friday 1:30 to 4:45 P. M.

On Friday afternoon there will be panel discussion sessions for six special fields of surgery as follows:

Orthopedic Surgery

GUY A. CALDWELL, M.D., F.A.C.S., New Orleans, *Moderator*

1:30 to 3:00 p.m.

Management of Established Non-Union of the Long Bones.

3:15 to 4:45 p.m.

Indications and Technique for Arthrodeses of the Joint of the Foot and Ankle in Post-traumatic Conditions.

Plastic Surgery

JEROME P. WEBSTER, M.D., F.A.C.S., New York, *Moderator*

1:30 to 3:00 p.m.

Plastic Surgery and the Treatment of Malignant Skin Disease.

3:15 to 4:45 p.m.

The Use of Skin Homografts.

Urology Surgery

GEORGE F. CAHILL, M.D., F.A.C.S., New York, *Moderator*

1:30 to 3:00 p.m.

Hydronephrosis Due to Upper Ureter Obstruction.

3:15 to 4:45 p.m.

Ureteral Intestinal Transplantation.

Thoracic Surgery

BRIAN B. BLADES, M.D., F.A.C.S., Washington, *Moderator*

1:30 to 3:00 p.m.

Surgery of the Heart and Great Vessels.

3:15 to 4:45 p.m.

Intrathoracic Tumors.

Neurological Surgery

ALFRED W. ADSON, M.D., F.A.C.S., Rochester, Minnesota, *Moderator*

1:30 to 3:30 p.m.

Chemical and Physical Diagnostic Aids in the Localization of Brain Tumor.

3:30 to 4:45 p.m.

Diagnosis and the Localization of Intraspinal Tumors.

Obstetrics and Gynecology Surgery

FRANKLIN L. PAYNE, M.D., F.A.C.S., Philadelphia, *Moderator*

1:30 to 3:30 p.m.

Carcinoma of the Uterine Cervix—Modern Concepts in Diagnosis and Treatment.

3:15 to 4:45 p.m.

Cesarean Section—Should the Latitude of its Indications be Broadened?

OPHTHALMOLOGY AND OTOLARYNGOLOGY

On Tuesday, Wednesday and Thursday separate programs are being planned for specialists in each of these two fields of surgery. Special emphasis will be given this year to hospital operative clinic programs. The detailed programs for the Ophthalmology section and for the Otolaryngology section will be announced later.

FORUM ON FUNDAMENTAL SURGICAL PROBLEMS

The Forum on Fundamental Surgical Problems will be held on Monday through Thursday afternoons, and Tuesday through Friday mornings. Brief reports of original clinical and experimental observations relating to the broad aspects of surgery and the surgical specialties will be presented, under the general direction of Dr. Owen H. Wangensteen, chairman of the committee, Forum on Fundamental Surgical Problems.

The Thursday afternoon session will be conducted by Dr. I. S. Ravdin of Philadelphia as a seminar on "Nutritional Problems Including a Consideration of Fluids and Electrolytes."

SYMPOSIUM ON CANCER

On Wednesday afternoon, from 2:00 to 5:00 o'clock, a Symposium on Cancer will be held. Speakers will include Dr. Hamilton Montgomery, of Rochester, Minnesota; Dr. Murray M. Copeland, of Washington, D.C., Dr. Herman L. Kretschmer, of Chicago; Dr. Arthur Purdy Stout, of New York; and Dr. Hayes Martin, of New York. Dr. Grantley W. Taylor, of Boston, chairman of the Cancer Committee, will preside.

SYMPOSIUM ON TRAUMA

An interesting program for the Symposium on Trauma on Tuesday afternoon, from 2:00 to 5:00 o'clock, is being developed under the direction of Dr. Robert H. Kennedy. Among the speakers will be Dr. Mather Cleveland, of New York; Dr. Harrison L. McLaughlin, of New York; and Dr. James Barrett Brown, of St. Louis.

HOSPITAL CONFERENCES

The twenty-eighth Hospital Standardization Conference will be held during the first 4 days of the Clinical Congress. Its opening meeting will constitute the first formal session of the Clinical Congress and will be for both surgeons and hospital representatives. Dr. Dallas B. Phemister, president of the College, will preside.

Hospital administrators, trustees, members of medical staffs, nurses, technicians, dietitians, and heads of the various hospital departments and their personnel, are invited to participate in the discussions at the hospital conferences which will be directed by leading authorities in the hospital field in the United States and Canada. The program will include formal sessions, panel discussions, round table conferences, symposia, and forums.

COMMITTEE ON ARRANGEMENTS AND EXECUTIVE COMMITTEE

The Chicago Committee on Arrangements and Executive Committee for the Clinical Congress are actively at work on arrangements for the program. The membership of these Committees follows:

Committee on Arrangements

Warren H. Cole, M.D., F.A.C.S., Chairman
Lester R. Dragstedt, M.D., F.A.C.S., Vice Chairman
Michael L. Mason, M.D., F.A.C.S., Secretary
Dallas B. Phemister, M.D., F.A.C.S., President and Regent of the College
William E. Adams, M.D., F.A.C.S.
James J. Callahan, M.D., F.A.C.S.
Fremont A. Chandler, M.D., F.A.C.S.
Edward A. Christofferson, M.D., F.A.C.S.
Vernon C. David, M.D., F.A.C.S.
Loyal Davis, M.D., F.A.C.S.
M. Edward Davis, M.D., F.A.C.S.
Paul W. Greeley, M.D., F.A.C.S.
Paul H. Holinger, M.D., F.A.C.S.
Sumner L. Koch, M.D., F.A.C.S.
Herman L. Kretschmer, M.D., F.A.C.S.
Walter G. Maddock, M.D., F.A.C.S.
Foster L. McMillan, M.D., F.A.C.S.
Karl A. Meyer, M.D., F.A.C.S.
Harry A. Oberhelman, M.D., F.A.C.S.
Willis J. Potts, M.D., F.A.C.S.
Charles B. Puestow, M.D., F.A.C.S.
Herbert E. Schmitz, M.D., F.A.C.S.
Derrick T. Vail, M.D., F.A.C.S.

Executive Committee

Warren H. Cole, M.D., Chairman
Lester R. Dragstedt, M.D., Vice Chairman
Michael L. Mason, M.D., Secretary
Dallas B. Phemister, M.D., President and Regent of the College
James J. Callahan, M.D.
Loyal Davis, M.D.
Walter G. Maddock, M.D.

PARTICIPATING HOSPITALS AND HOSPITAL CLINICS COMMITTEE

A list of the participating hospitals and hospital clinics committee follows:

Augustana Hospital: OSCAR E. NADEAU, M.D., F.A.C.S.
Children's Memorial Hospital: PAUL F. FOX, M.D., F.A.C.S.
Cook County Hospital: MANUEL E. LICHTENSTEIN, M.D., F.A.C.S.
Evanston Memorial Hospital: FREDERICK CHRISTOPHER, M.D., F.A.C.S.
Illinois Eye and Ear Infirmary: MAURICE D. PEARLMAN, M.D.
Lewis Memorial Maternity Hospital: HERBERT E. SCHMITZ, M.D., F.A.C.S.
Mercy Hospital-Loyola University Clinics: JOHN B. O'DONOGHUE, M.D., F.A.C.S.
Michael Reese Hospital: MORRIS L. PARKER, M.D., F.A.C.S.
Mount Sinai Hospital: DAVID A. WILLIS, M.D., F.A.C.S.
Passavant Memorial Hospital: WALTER W. CARROLL, M.D., F.A.C.S.
Presbyterian Hospital: FRANCIS H. STRAUS, M.D., F.A.C.S.
Provident Hospital: ULYSSES GRANT DAILEY, M.D., F.A.C.S.
Research and Educational Hospitals (University of Illinois): JOHN T. REYNOLDS, M.D., F.A.C.S.
St. Elizabeth's Hospital: MARTIN GIRARD LUKEN, M.D., F.A.C.S.
St. Joseph Hospital: LEONARD KRATZ, M.D., F.A.C.S.
St. Luke's Hospital: FOSTER L. MCMILLAN, M.D., F.A.C.S. Assistant: JOHN T. REYNOLDS, M.D., F.A.C.S.
St. Mary of Nazareth Hospital: ANTHONY S. SAMPOLINSKI, M.D., F.A.C.S.
University of Chicago Clinics
Albert Merritt Billings Hospital: J. GARROTT ALLEN, M.D., F.A.C.S.

Bobs Roberts Memorial Hospital for Children: J. GARROTT ALLEN, M.D., F.A.C.S.
Chicago Lying-in Hospital and Dispensary: WILLIAM DRECKMANN, M.D.
Home for Destitute Crippled Children: J. GARROTT ALLEN, M.D., F.A.C.S.
Wesley Memorial Hospital: EARL O. LATIMER, M.D., F.A.C.S.
Hines Veterans Administration Hospital: CHARLES B. PUESTOW, M.D., F.A.C.S. Assistant: JAMES H. CROSS, M.D., F.A.C.S.

SPECIAL COMMITTEE ON TELEVISION

Foster L. McMillan, M.D., F.A.C.S., St. Lukes Hospital, Chairman
Burton C. Kilbourne, M.D.
Charles E. Shannon, M.D., F.A.C.S.

GENERAL AND PROGRAM COMMITTEES

The Clinical Congress general committee which operates under the Administrative Board of the College, consists of Dr. Malcolm T. MacEachern, chairman, Miss Eleanor K. Grimm, secretary, Doctors Bowman C. Crowell, Charles F. Branch, George H. Miller and H. Prather Saunders, and Mr. Edward G. Sandrok, Mr. James S. Shannon, and Miss Laura G. Jackson.

The Clinical Congress Committee on Program consists of Dr. Frederick A. Coller, chairman, and Doctors Henry W. Cave, Evarts A. Graham, and Alton Ochsner.

The Advisory Committee on Programs consists of Dr. George H. Miller, chairman, and Doctors Warren H. Cole, Sumner L. Koch, Michael L. Mason, Charles B. Puestow, Bowman C. Crowell, H. Prather Saunders, Charles F. Branch, and Malcolm T. MacEachern.

MEDICAL MOTION PICTURES

The showing of medical motion pictures each day will again be a popular feature of the Clinical Congress. The latest available films on surgery and related subjects will be presented. Special showings will be arranged of medical motion pictures in the fields of ophthalmology and otorhinolaryngology. Both sound and silent films will be shown, all of which will have been approved by the Committee on Motion Pictures.

Some of the newer medical motion pictures which have been or are being produced under Directing Committees of the College, will be presented during the Clinical Congress. Among these will be the film entitled "Injuries of the Peripheral Nerves" directed by Dr. Loyal Davis, under a grant from the Johnson & Johnson Research Foundation. A première showing of this particular film will take place in the Murphy Memorial Auditorium of the College at the time of the Congress in October.

TECHNICAL AND EDUCATIONAL EXHIBITION

The Technical and Educational Exhibits will be held in the Exhibition Hall on the lower level of The Stevens. There will be represented leading manufacturers of surgical instruments, of x-ray apparatus, of sterilizers, of operating room lights, of ligatures, of dressings, of hospital apparatus and supplies of all kinds, and of pharmaceuticals, and publishers of medical books.

There will also be presented exhibits depicting the work of the College.

ADVANCE REGISTRATION

Surgeons who wish to attend the Congress should register in advance. Advance registration will greatly expedite the procedure of registering. No registration fee will be charged Fellows whose dues are paid to December 31, 1948. For endorsed Junior and Senior Candidates, the fee will be $5.00. Non-Fellows who after individual consideration are permitted to register, will pay a fee of $10.00. No registration fee will be required of initiates of the class of 1949.

HOTEL RESERVATIONS

It is desirable to make hotel reservations as early as possible. In making these, communications should be addressed to the Convention Housing Bureau, 105 West Madison Street, Chicago, stating that you will be attending the Clinical Congress of the American College of Surgeons. All hotel reservations, both for surgeons and hospital representatives, are to clear through this Bureau. No correspondence should be sent directly to the hotels. A form for reservations was enclosed in the letter recently sent to Fellows. Choice of hotels may be designated.

A list of the principal participating hotels and minimum rates follows:

Chicago Hotels	Single	Double
Atlantic	$3.50	$5.00
Bismarck	5.00	8.00
Brevoort	3.50	6.00
Chicagoan	3.75	5.50
Drake	4.50	7.50
Eastgate	3.50	5.50
Hamilton	4.00	6.00
Harrison	3.00	4.00
Knickerbocker	5.00	8.00
Maryland	4.00	6.00
Midland	3.00	4.50
Palmer House	4.00	8.00
Sheraton	3.85	6.40
Stevens	4.50	7.00

SIXTH INTER-AMERICAN CONGRESS OF SURGERY

Chicago, Illinois, October 17 to 23, 1949

Separate Sessions—October 21, 22, and 23

THE Sixth Inter-American Congress of Surgery will meet as a part of the Thirty-fifth Clinical Congress of the American College of Surgeons from October 17 to 21, with headquarters at The Stevens in Chicago, and will continue on October 21, 22, and 23 with its own business, scientific, and social sessions, most of which will be held in the John B. Murphy Memorial Auditorium of the College at 50 East Erie Street.

The surgical societies of the following countries, in addition to the United States, are members of the Association of Inter-American Congresses of Surgery: Argentina, Bolivia, Brazil, Chile, Cuba, Ecuador, Mexico, Panama, Paraguay, Peru, and Uruguay. The American College of Surgeons joined the association by vote of the Board of Regents on June 27, 1943. This action was preceded by an invitation from Dr. Luis Vargas Salcedo of Santiago, Chile, to send two delegates as guests of honor to the First Inter-American Congress of Surgery, held in Santiago November 15 to 19, 1942. Dr. Leo Eloesser, of San Francisco, attended as delegate; and it was upon his enthusiastic recommendation that the College joined the association. He also attended the second Congress, in Buenos Aires, October 10 to 15, 1943. Dr. Alton Ochsner, of New Orleans, was delegate to the third Congress, in Montevideo, Uruguay, October 1 to 6, 1946. No delegates were sent to the fourth Congress, held in Rio de Janeiro in 1947. Dr. E. Payne Palmer, of Phoenix, and Dr. Hu Crim Myers, of Philippi, West Virginia, were delegates and co-relators at the fifth Congress, held in La Paz, Bolivia, October 17 to 21, 1948.

Dr. Frederick A. Coller, who will be inducted on October 17 as President of the American College of Surgeons, will, as President of the signatory society of surgeons in the host country, serve as President of the Sixth Inter-American Congress of Surgery. Dr. Arnaldo Caviglia, of Buenos Aires, is Secretary-General of the association, and will set up an office in Chicago prior to and during the meeting. The following committees will aid in the arrangements:

COMMITTEES ON INTER-AMERICAN RELATIONS, AMERICAN COLLEGE OF SURGEONS

General Committee on Inter-American Relations

IRVIN ABELL, Louisville, *Chairman*
ALFRED BLALOCK, Baltimore
FRANCIS P. CORRIGAN, Washington
LEO ELOESSER, San Francisco
RUDOLPH MATAS, New Orleans
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ALTON OCHSNER, New Orleans, *Chairman*
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DALLAS B. PHEMISTER, Chicago

THE PROGRAM

A preliminary outline of the program for the Sixth Inter-American Congress of Surgery follows:

Friday morning, October 21

Inaugural Ceremony.

Friday afternoon, October 21

Delegates may attend the specialty panels of the Clinical Congress.

Saturday morning, October 22

Main Theme: Acute Craniocerebral Trauma.
Relator: E. JEFFERSON BROWDER, M.D., F.A.C.S., Brooklyn, New York, U.S.A.
Co-relators: To be appointed by each member country.

Saturday afternoon, October 22

Main Theme: Treatment of Injuries in the Region of the Ankle with Complications and Sequelae.
Relator: HARRISON L. MCLAUGHLIN, M.D., F.A.C.S., New York, New York, U.S.A.
Co-relators: To be appointed by each country.

Saturday evening, October 22

Official Banquet.

Sunday morning, October 23

Business Session.

Sunday afternoon, October 23

Main Theme: Pulmonary Carcinoma.
Relator: EVARTS A. GRAHAM, M.D., F.A.C.S., St. Louis, Missouri, U.S.A.
Co-relators: To be appointed by each member country.

THIRTEENTH CONGRESS, INTERNATIONAL SOCIETY OF SURGERY

(Société Internationale de Chirurgie)

New Orleans, Louisiana, U.S.A., October 9 to 15, 1949

THE following announcement has been received from Dr. L. Dejardin, Secretary-General of the International Society of Surgery:

Plans for the Thirteenth Congress of the International Society of Surgery, which will take place in New Orleans, Louisiana, under the Presidency of Professor George Grey Turner, of London, England, are now in course of preparation.

The scientific program was settled by the General Assembly at the last Congress in London, held in September, 1947. This body, at the recommendation of the Scientific Committee, also accepted two additional subjects, and decided who should open each discussion. The final arrangements were as follows:

1. Surgery and Pathology of the Pancreas, Especially in Relation to Its Endocrine Function. Opened by PROFESSOR IAN AIRD, London.
2. Surgery of the Parathyroid Glands. Opened by DR. PAOLUCCI, Rome.
3. Surgery of the Suprarenal Glands. Opened by DR. M. R. FONTAINE, Strasburg.
4. Pathology and Surgery of the Pituitary Glands. Opened by DR. M. P. MARTIN, Brussels.
5. Treatment of Postoperative Thrombosis and Its Sequelae. Opened by DR. ALTON OCHSNER, New Orleans, and DR. MICHAEL DE BAKEY, Houston.
6. Causes of Recurrence after Operations on the Biliary Tract. Opened by DR. M. R. DEMEL, Vienna.

In addition, the American Organizing Committee has arranged that two or three days of the meeting shall be devoted to the presentation of shorter papers on subjects of immediate interest.

The complete program, both scientific and social, will be circulated in due course.

The program is being formulated by Vice President Evarts A. Graham, of St. Louis, Missouri.

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GORDON GORDON-TAYLOR, London, England, *Vice-President*
P. MATHIEU, Paris, France, *Vice-President*
R. DOS SANTOS, Lisbon, Spain, *Vice-President*
EVARTS A. GRAHAM, St. Louis, Missouri, U.S.A., *Vice-President*
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J. VERHOOGEN, Brussels, Belgium, *President of International Committee*
LEO A. M. DEJARDIN, Brussels, Belgium, *Secretary-General*
PAUL E. LORTHIOIR, Brussels, Belgium, *Treasurer*
G. SPEHL, Brussels, Belgium, *Editor, "Journal International de Chirurgie"*
I. MIMS GAGE, New Orleans, Louisiana, *Secretary of the 13th Congress*

NATIONAL COMMITTEE FOR THE UNITED STATES

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DANIEL C. ELKIN, Atlanta, Georgia
ALTON OCHSNER, New Orleans, Louisiana

Inquiries should be directed to:

DR. L. DEJARDIN, *Secretary-General*
International Society of Surgery
141, Rue Belliard, Brussels, Belgium.